```
=> file hcaplus; d que l24; d que l26
FILE 'HCAPLUS' ENTERED AT 14:48:24 ON 05 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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```


FILE COVERS 1907 - 5 Nov 2004 VOL 141 ISS 20
FILE LAST UPDATED: 4 Nov 2004 (20041104/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L1        25685 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PRIMERS (NUCLEIC ACID)"+PFT/C
                T
L3          685 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "NUCLEOTIDES, BIOLOGICAL
                STUDIES"/CT (L) (FINGERPRINT? OR CLEAV? OR PRIMER)
L5        16194 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GENETIC METHODS/CT
L6          286 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNA FOOTPRINTING/CT
L7         6318 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNA SEQUENCE ANALYSIS/CT
L8        44503 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GENETIC MAPPING/CT
L9           60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L3 AND (L5 OR L6 OR L7
                OR L8)
L13           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND CLEAV?
L14          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (SIZE? OR SIZI? OR
                SIZA? OR LENGTH)
L16      361760 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SUGAR OR URACIL OR RIBOSE OR
                ?AVIDIN?
L17          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L3 AND L16
L18     4343965 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLASS OR SILICON OR POLYSTYREN
                E OR ALUMINUM OR STEEL OR IRON OR COPPER OR NICKEL OR SILVER
                OR GOLD
L19          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L3 AND L18
L20          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 OR L14 OR L17 OR L19
L21          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND PY<1999
L22          17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND PRY<1999
L23          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 OR L22
L24          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 NOT (TUBERCULOSIS OR
                RHESUS OR SEX OR MANGANESE OR WATERMELON)/TI


L1        25685 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PRIMERS (NUCLEIC ACID)"+PFT/C
                T
L3          685 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "NUCLEOTIDES, BIOLOGICAL
                STUDIES"/CT (L) (FINGERPRINT? OR CLEAV? OR PRIMER)
L5        16194 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GENETIC METHODS/CT
```

```
L6          286 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNA FOOTPRINTING/CT
L7         6318 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNA SEQUENCE ANALYSIS/CT
L8        44503 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GENETIC MAPPING/CT
L9           60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L3 AND (L5 OR L6 OR L7
                   OR L8)
L13           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND CLEAV?
L14          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (SIZE? OR SIZI? OR
                   SIZA? OR LENGTH)
L16      361760 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SUGAR OR URACIL OR RIBOSE OR
                   ?AVIDIN?
L17          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L3 AND L16
L18     4343965 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLASS OR SILICON OR POLYSTYREN
                   E OR ALUMINUM OR STEEL OR IRON OR COPPER OR NICKEL OR SILVER
                   OR GOLD
L19          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 AND L3 AND L18
L20          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 OR L14 OR L17 OR L19
L21          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND PY<1999
L22          17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND PRY<1999
L23          26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 OR L22
L25          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 NOT L23
L26          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 NOT (CIRCULAR OR HIV OR
                   MRNA OR ARRAY)


=> s l24 or 126
L67          31 L24 OR L26

=> file biosis; d que l36
FILE 'BIOSIS' ENTERED AT 14:48:48 ON 05 NOV 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 3 November 2004 (20041103/ED)

FILE RELOADED: 19 October 2003.


L30        31638 SEA FILE=BIOSIS ABB=ON  PLU=ON  PRIMERS
L31       307262 SEA FILE=BIOSIS ABB=ON  PLU=ON  NUCLEIC OR NUCLEOTI? OR
                   OLIGONUCLE?
L32       100617 SEA FILE=BIOSIS ABB=ON  PLU=ON  CLEAV?
L35           10 SEA FILE=BIOSIS ABB=ON  PLU=ON  L30 (5A) L31 (10A) L32
L36            2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L35 AND SIZING/TI


=> file medline; d que l43
FILE 'MEDLINE' ENTERED AT 14:48:55 ON 05 NOV 2004

 FILE LAST UPDATED: 4 NOV 2004 (20041104/UP).  FILE COVERS 1950 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details.

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
```

MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L37        56801 SEA FILE=MEDLINE ABB=ON  PLU=ON  DNA PRIMERS/CT
L41         1212 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37/MAJ
L42        14039 SEA FILE=MEDLINE ABB=ON  PLU=ON  CLEAV?/TI
L43            4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L41 AND L42
```

```
=> => file embase; d que l48
FILE 'EMBASE' ENTERED AT 14:50:01 ON 05 NOV 2004
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```

FILE COVERS 1974 TO 4 Nov 2004 (20041104/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L44         3955 SEA FILE=EMBASE ABB=ON  PLU=ON  PRIMER DNA/CT
L45          857 SEA FILE=EMBASE ABB=ON  PLU=ON  L44/MAJ
L46        12719 SEA FILE=EMBASE ABB=ON  PLU=ON  CLEAV?/TI
L47            3 SEA FILE=EMBASE ABB=ON  PLU=ON  L45 AND L46
L48            1 SEA FILE=EMBASE ABB=ON  PLU=ON  L47 AND DESIGN/TI
```

```
=> file wpix; d que l66
FILE 'WPIX' ENTERED AT 14:50:18 ON 05 NOV 2004
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FILE LAST UPDATED:          4 NOV 2004      <20041104/UP>
MOST RECENT DERWENT UPDATE:     200471        <200471/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
    http://thomsonderwent.com/coverage/latestupdates/          <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/              <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
    DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
    FIRST VIEW - FILE WPIFV.
    FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv  <<<

>>> NEW DISPLAY FORMAT HITSTR ADDED ALLOWING DISPLAY OF
    HIT STRUCTURES WITHIN THE BIBLIOGRAPHIC DOCUMENT  <<<
```

>>> SMILES and ISOSMILES strings are no longer available as
Derwent Chemistry Resource display fields <<<

L49 8606 SEA FILE=WPIX ABB=ON PLU=ON PRIMER (5A) (DNA OR NUCLEOT? OR OLIGONUCLEOT? OR NUCLEIC)
L50 7115 SEA FILE=WPIX ABB=ON PLU=ON FINGERPRINT?
L51 18037 SEA FILE=WPIX ABB=ON PLU=ON CLEAV?
L52 47537 SEA FILE=WPIX ABB=ON PLU=ON MAP OR MAPP?
L53 2139 SEA FILE=WPIX ABB=ON PLU=ON SEQUENCE (2A) (ANALYS? OR ANALYZ?)
L57 12 SEA FILE=WPIX ABB=ON PLU=ON L49 AND L51 AND L50
L58 38 SEA FILE=WPIX ABB=ON PLU=ON L49 AND L51 AND L52
L59 11 SEA FILE=WPIX ABB=ON PLU=ON L58 AND AMPLIF?/TI
L60 34 SEA FILE=WPIX ABB=ON PLU=ON L49 AND L51 AND L53
L61 32 SEA FILE=WPIX ABB=ON PLU=ON L60 NOT (L59 OR L57)
L62 54 SEA FILE=WPIX ABB=ON PLU=ON L57 OR L59 OR L61
L63 7 SEA FILE=WPIX ABB=ON PLU=ON L62 AND PY<1999
L64 22 SEA FILE=WPIX ABB=ON PLU=ON L62 AND PRY<1999
L65 22 SEA FILE=WPIX ABB=ON PLU=ON L63 OR L64
L66 17 SEA FILE=WPIX ABB=ON PLU=ON L65 NOT (ELONGA? OR PHOSPHOR? OR SPOTS OR TEMPLATES OR BLOOD)/TI

=> dup rem l43 l66 l67 l36 l48
FILE 'MEDLINE' ENTERED AT 14:54:18 ON 05 NOV 2004

FILE 'WPIX' ENTERED AT 14:54:18 ON 05 NOV 2004
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FILE 'BIOSIS' ENTERED AT 14:54:18 ON 05 NOV 2004
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FILE 'EMBASE' ENTERED AT 14:54:18 ON 05 NOV 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.
PROCESSING COMPLETED FOR L43
PROCESSING COMPLETED FOR L66
PROCESSING COMPLETED FOR L67
PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L48
L68 54 DUP REM L43 L66 L67 L36 L48 (1 DUPLICATE REMOVED)
ANSWERS '1-4' FROM FILE MEDLINE
ANSWERS '5-21' FROM FILE WPIX
ANSWERS '22-51' FROM FILE HCAPLUS
ANSWERS '52-53' FROM FILE BIOSIS
ANSWER '54' FROM FILE EMBASE

=> d ibib ed ab l61 1-4; d ibib ab abex l68 5-21; d ibib ed ab l68 22-54

L61 ANSWER 1 OF 32 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-507017 [48] WPIX
DOC. NO. NON-CPI: N2004-400631
DOC. NO. CPI: C2004-187700

TITLE: New guide oligonucleotide comprising single-stranded or partially double-stranded nucleic acid, which comprises target complementary region, constant region, identifier sequence, and restriction site, useful in analyzing gene expression.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): FU, G
PATENT ASSIGNEE(S): (FUGG-I) FU G
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004053159	A2	20040624	(200448)*	EN	47

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004053159	A2	WO 2003-GB5271	20031203

PRIORITY APPLN. INFO: GB 2002-28614 20021207
ED 20040728
AB WO2004053159 A UPAB: 20040728
NOVELTY - A guide oligonucleotide comprising single-stranded or partially double-stranded nucleic acid, which comprises target complementary region, constant region, identifier sequence, and at least one restriction site, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for analyzing polynucleotides in a sample.
USE - The guide oligonucleotides are useful in analyzing polynucleotides in a sample quantitatively or in analyzing gene expression. The method is useful in medical and scientific research, drug discovery, and in genetic analysis in a host of applied fields.
Dwg.0/4

L61 ANSWER 2 OF 32 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-440342 [41] WPIX
DOC. NO. CPI: C2004-164948
TITLE: Reducing the complexity of a genomic DNA, useful for discovering single nucleotide polymorphisms or for genotyping individuals, comprises performing semi-specific amplification of specific fragments of genomic DNA.
DERWENT CLASS: B04 D16
INVENTOR(S): DONG, S; SU, X
PATENT ASSIGNEE(S): (AFFY-N) AFFYMETRIX INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

US 2004110153 A1 20040610 (200441)* 29

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004110153	A1	US 2002-316811	20021210

PRIORITY APPLN. INFO: US 2002-316811 20021210
ED 20040629
AB US2004110153 A UPAB: 20040629
NOVELTY - Reducing the complexity of a first nucleic acid sample to produce a second nucleic acid sample, where the second nucleic acid sample comprises target sequences, comprises performing semi-specific amplification of specific fragments of genomic DNA.

DETAILED DESCRIPTION - The above method comprises:

(a) fragmenting a first nucleic acid sample to create a population of fragments;

(b) modifying the ends of the fragments to generate a population of modified fragments;

(c) hybridizing to the modified fragments a first primer comprising a 5' first common sequence and a 3' region that is complementary to the modified fragments;

(d) extending the first primer to generate extended first primers that are complementary to the modified fragments and comprise the first common sequence;

(e) hybridizing target specific primers to the extended first primers where each target specific primer comprises a second common sequence and each species of target specific primer comprises a region that hybridizes to an extended first primer upstream of a region of interest in one of the target sequences;

(f) extending the target specific primers to generate extended target specific primers, where each extended target specific primer comprises the second common sequence at the 5' end and the complement of the first common sequence at the 3' end; and

(g) amplifying the extended target specific **primers** to generate the second **nucleic** acid sample using a first amplification primer comprising at least part of the first common sequence and a second amplification primer comprising at least part of the second common sequence.

INDEPENDENT CLAIMS are also included for:

(1) genotyping a collection of polymorphic sequences or polymorphic regions, or genotyping at least one polymorphic position in a collection of target sequences; and

(2) enriching a nucleic acid population for target sequences.

USE - The methods are useful for reducing the complexity of a nucleic acid sample or for analyzing complex samples of nucleic acids, such as genomic DNA, in a rapid, effective and inexpensive manner. These may be used for discovering single nucleotide polymorphisms, for genotyping individuals, for diagnosing diseases and predisposition to a disease, or in pharmacogenomics or forensics.

Dwg.0/8

L61 ANSWER 3 OF 32 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-400661 [37] WPIX
CROSS REFERENCE: 2003-018656 [01]; 2003-018657 [01]; 2003-156728 [15]; 2003-865210 [80]

DOC. NO. CPI: C2004-150095
TITLE: Novel amylase polypeptide useful in starch to fructose processing, treating animal feeds and additives, paper treatment process and waste treatment.
DERWENT CLASS: C06 D16 D17
INVENTOR(S): ABOUSHADI, N; GARRETT, J B; GRAY, K A
PATENT ASSIGNEE(S): (DIVE-N) DIVERSA CORP
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004042006	A2	20040521	(200437)*	EN	222
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003285906	A1	20040607	(200469)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004042006	A2	WO 2003-US33150	20031015
AU 2003285906	A1	AU 2003-285906	20031015

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003285906	A1 Based on	WO 2004042006

PRIORITY APPLN. INFO: US 2002-423626P 20021031
ED 20040611
AB WO2004042006 A UPAB: 20041027
NOVELTY - An isolated or recombinant amylase polypeptide (I) comprising 618 amino acid sequence (S1), a sequence having 90% identity to 617 amino acid sequence (S2), 60% identity to 621 amino acid sequence (S3), 50% identity to 677 amino acid sequence (S4), 70% identity to 592 amino acid sequence (S5) or 80% identity to 706 amino acid sequence (S6), is new. All sequences are fully defined in specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid (IIa) showing sequence identities to 1854, 1854, 1866, 2034, 1779, 2121 nucleotide sequences (S8-S12) defined in the specification, and comprising a sequence that hybridizes under stringent conditions to (S7)-(S12) where (II) is isolated or recombinant and encodes at least one polypeptide having an amylase activity;

(2) a nucleic acid probe (III) for identifying nucleic acid encoding amylase, where (III) comprises 10 consecutive bases of (S7)-(S12) and (III) identifies the nucleic acid by binding or hybridization or comprises (S7), sequence having 95% identity to (S8), 70% identity to (S9), 60% identity to (S10), 80% identity to (S11), or 90% identity to (S12), where the identity is over a region of 100 residues;

(3) an amplification primer sequence pair (IV) for amplifying a nucleic acid encoding a polypeptide having an amylase activity, where (IV)

is capable of amplifying (S7)-(S12) or their subsequence;

(4) an expression cassette (V) comprising (IIa) or (IIb);

(5) a vector (VI) comprising (IIa) or (IIb);

(6) a cloning vehicle (VII) comprising (VI), where (VII) comprises a viral vector, plasmid, phage, phagemid, cosmid, fosmid, bacteriophage or artificial chromosome;

(7) a transformed cell (VIII) comprising (VI) or (IIa)/(IIb);

(8) a transgenic non-human animal (IX) comprising (IIa) or (IIb);

(9) a transgenic plant (X) comprising (IIa) or (IIb);

(10) a transgenic seed (XI) comprising (IIa) or (IIb);

(11) an antisense oligonucleotide (XII) comprising a nucleic acid sequence complementary to or capable of hybridizing under stringent conditions to (IIa) or (IIb);

(12) an isolated or recombinant polypeptide (XIII) comprising (I) and lacking a signal sequence;

(13) a protein preparation (XIV) comprising (I), where the protein preparation comprises a liquid, a solid or a gel;

(14) a heterodimer (XV) comprising (I) and a second domain;

(15) a homodimer (XVI) comprising (I);

(16) an immobilized polypeptide (XVII) having an amylase activity, where the polypeptide comprises (I);

(17) an array comprising immobilized (I), (II), or (XV);

(18) an isolated or recombinant antibody (XVIII) that specifically binds to (I) or to a polypeptide encoded by (II);

(19) a hybridoma comprising (XVIII);

(20) a food supplement for an animal or an edible enzyme delivery matrix;

(21) preparation of (I);

(22) a computer system comprising a processor and a data storage device where the data storage device has stored in it, the sequence of (I) or the sequence of polypeptide encoded by (II);

(23) a computer readable medium having stored in it, the sequence of (I) or the sequence of polypeptide encoded by (II);

(24) identifying a feature in a sequence using a computer program which identifies one or more features in a sequence, where the sequence is a polypeptide or nucleic acid sequence, and the polypeptide sequence is (I) or a polypeptide encoded by (I);

(25) comparing first sequence to a second sequence using a computer program which compares sequences, where the first sequence comprising a polypeptide or nucleic acid sequence, and the polypeptide sequence is (I) or a polypeptide encoded by (I);

(26) isolating or recovering nucleic acid encoding (I) from an environmental sample;

(27) modifying codons in a nucleic acid encoding an amylase polypeptide to increase its expression in a host cell,

(28) modifying codons in a nucleic acid encoding a polypeptide having an amylase activity to decrease its expression in a host cell;

(29) producing a library of nucleic acids;

(30) making a small molecule;

(31) whole cell engineering of new or modified phenotypes by using real-time metabolic flux analysis;

(32) increasing thermotolerance or thermostability of an amylase polypeptide which involves glycosylating the polypeptide;

(33) overexpressing a recombinant amylase polypeptide in a cell;

(34) a detergent composition or anti-staling composition;

(35) an amplification primer pair which comprises a first member having a sequence as set forth by the first (the 5') 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or more residues of (II), and a second member having a sequence as set forth by about the

first (the 5') 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or more residues of the complementary strand of the first member;

(36) an amylase-encoding nucleic acid (XIX) generated by amplification of polynucleotide using the primer pair as described above; and

(37) an isolated or recombinant protease encoded by (XIX).

USE - (I) or (II) is useful for producing an antiamylase antibody, and for determining whether a test compound specifically binds to a polypeptide. (I) or a polypeptide encoded by (II) is useful for identifying an amylase substrate, identifying a polypeptide having amylase activity, and for identifying a modulator of amylase activity.

(I) or polypeptide encoded by (II) is also useful for modifying a small molecule, determining a functional fragment of an amylase enzyme, hydrolyzing starch (comprising alpha -1,4- or alpha -1,6-glucosidic bond), liquefying or removing starch from a composition, treating lignocellulosic fibers, producing high-maltose or a high-glucose syrup, improving flow of starch containing production fluids (from a subterranean formation), preventing staling of baked product, washing an object, hydrolyzing a starch in a feed or food (comprising rice, corn, barley, wheat, legumes, or potato) prior to consumption by an animal, textile desizing, deinking of paper or fibers, or in brewing or alcohol production.

(II) is useful for generating a variant of a nucleic acid encoding a polypeptide with an amylase activity, and for making a transgenic plant, and for expressing a heterologous nucleic acid sequence in plant cell.

(IV) is useful for amplifying a nucleic acid encoding polypeptide having an amylase activity which involves amplification of template nucleic acid with (IV). (XII) is useful for inhibiting the translation of an amylase message in a cell which involves administering to the cell or expressing in the cell (XII).

(XVIII) is useful for isolating or identifying a polypeptide with amylase activity (all claimed).

ADVANTAGE - (I) is thermostable and thermotolerant (claimed).

Dwg.0/4

L61 ANSWER 4 OF 32 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-213927 [20] WPIX
DOC. NO. CPI: C2004-084692
TITLE: New oligonucleotide tagged nucleoside triphosphates, useful for genetic analysis and detecting differential gene expression.
DERWENT CLASS: B04 D16
INVENTOR(S): KUMAR, S; NELSON, J; RAO, S; SOOD, A
PATENT ASSIGNEE(S): (KUMA-I) KUMAR S; (NELS-I) NELSON J; (RAOS-I) RAO S; (SOOD-I) SOOD A; (AMSH) AMERSHAM BIOSCIENCES CORP
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004038215	A1	20040226	(200420)*		23
WO 2004018712	A1	20040304	(200420)	EN	
RW:	AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW				

AU 2003262791 A1 20040311 (200457)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004038215	A1	US 2002-226734	20020823
WO 2004018712	A1	WO 2003-US26339	20030821
AU 2003262791	A1	AU 2003-262791	20030821

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003262791	A1 Based on	WO 2004018712

PRIORITY APPLN. INFO: US 2002-226734 20020823
ED 20040324
AB US2004038215 A UPAB: 20040324
NOVELTY - Oligonucleotide tagged nucleoside triphosphates (OTNTP) (I) are new.

DETAILED DESCRIPTION - Oligonucleotide tagged nucleoside triphosphates (OTNTP) of formula (I) are new.

R, R' = H, OH, OCH3, CH3, N3, SH, NCO, NCS, SCN, NH2, F, Cl or NR''R'';

R'' = H or 1-5C alkyl;

X = O, S, CH3 or BH3;

Base = uracil, cytosine, thymine, adenine, guanine, hypoxanthine, 2-aminopurine, 2,6-diaminopurine, xanthene, deazaadenine, deazaguanine or their analogs;

Linker = alkynyl, alkenyl, alkyl, alkylaryl, aryl or arylalkyl all containing one or more heteroatoms from N, O, S or P;

N = ribose, deoxyribose or a natural or unnatural deoxyribonucleoside or ribonucleoside (optionally containing a detectable moiety); and

n = 2-100.

N is linked to at least one other N by phosphodiester, phosphorothioate, alkyl phosphonate or other linkages.

INDEPENDENT CLAIMS are also included for the following:

(1) compounds of formulae (II)-(IV);

(2) a method of genetic analysis (M1) comprising:

(a) mixing a sample of DNA or RNA target with a sequence specific primer in an aqueous buffer;

(b) adding a nucleic acid polymerase, a set of four OTNTP terminators (I) bearing either:

(i) unique oligonucleotide sequences;

(ii) a detectable label; or

(iii) a donor and acceptor dye specific for a particular base;

(c) incubating the mixture at a temperature an time sufficient for polymerase activity to incorporate an OTNTP; and

(d) detecting the OTNTP incorporated by:

(i) hybridization with a labelled probe;

(ii) detecting the label attached to OTNTP; or

(iii) exciting the donor dye and measuring emission from the acceptor dye;

(3) a method of genetic analysis (M2) comprising:

(a) mixing a sample of DNA or RNA target with a sequence specific primer in an aqueous buffer;

(b) adding a polymerase and a set of OTNTP terminators (I) to form a mixture and incubating to allow the polymerase to incorporate an OTNTP;

(c) amplifying the OTNTP oligonucleotide sequence; and
(d) identifying the amplified sequence;
(4) incorporating (M3) an OTNTP (I) into DNA or RNA using a terminal nucleosidyl transferase comprising
(a) mixing a biological sample containing DNA and/or RNA with an OTNTP and a terminal nucleosidyl transferase in a buffer; and
(b) incubating the mixture;
(5) incorporating (M4) an OTNTP (I) into DNA using a DNA polymerase or reverse transcriptase comprising
(a) mixing a DNA or RNA template and a primer in an aqueous buffer;
(b) adding a DNA polymerase or reverse transcriptase and one or more OTNTP (I); and
(c) incubating the mixture;
(6) incorporating (M5) an OTNTP (I) into RNA using an RNA polymerase or primase comprising
(a) mixing a DNA template and RNA polymerase or primase in an aqueous buffer;
(b) adding at least one OTNTP (I); and
(c) incubating the mixture;
(7) preparations of (I);
(8) separating a specific DNA or RNA sequence comprising:
(a) incorporating an OTNTP carrying a specific oligonucleotide sequence as an affinity tag into DNA or RNA;
(b) incubating with a solid support carrying the complementary oligonucleotide sequence to capture the tagged DNA or RNA; and
(c) removing the uncaptured materials by washing; and
(9) quantifying (M6) differential gene expression in two different tissues comprising;
(a) separately making cDNA copies of messages using M4 in two tissue samples using at least two OTNTP, where the OTNTP has a different oligo tag specific to each tissue sample;
(b) mixing the two samples and hybridizing the cDNA to DNA or an oligonucleotide chip;
(c) detecting the site; and
(d) quantifying the amount of each oligonucleotide tag.
Ra = non-reactive polar or non-polar group;
Rb = alkyl or cyanoethyl;
Rc = 1-6C alkyl; or
RcRc = 5-7 membered cyclic structure; and
Linker' = optionally branched, optionally saturated acyclic, cyclic or aromatic compound, optionally containing one or more heteroatoms from N, O, S and P.
USE - The nucleoside triphosphates are used for genetic analysis.
Dwg.0/10

L68 ANSWER 5 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN DUPLICATE 1
ACCESSION NUMBER: 1997-021231 [02] WPIX
DOC. NO. CPI: C1997-006943
TITLE: Analysis of **nucleic** sequence size - by producing **primer** extension prods. using a primer having a **cleavable** site and analysis by mass spectrometry.
DERWENT CLASS: B04 D16
INVENTOR(S): BECKER, C H; MONFORTE, J A; POLLART, D J; SHALER, T A
PATENT ASSIGNEE(S): (STRI) SRI INT
COUNTRY COUNT: 23

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9637630	A1	19961128	(199702)*	EN	109<--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA CN JP KR					
AU 9656352	A	19961211	(199713)		<--
US 5700642	A	19971223	(199806)		38<--
EP 828855	A1	19980318	(199815)	EN	<--
R: DE FR GB IT NL					
AU 695705	B	19980820	(199845)		<--
US 5830655	A	19981103	(199851)		<--
JP 11505127	W	19990518	(199930)		133
EP 828855	B1	19991215	(200003)	EN	
R: DE FR GB IT NL					
DE 69605669	E	20000120	(200011)		
KR 99021950	A	19990325	(200023)		
CN 1191575	A	19980826	(200275)		<--
CA 2220418	C	20030603	(200344)	EN	
JP 3437184	B2	20030818	(200356)		57

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9637630	A1		WO 1996-US6116	19960430
AU 9656352	A		AU 1996-56352	19960430
US 5700642	A		US 1995-445751	19950522
EP 828855	A1		EP 1996-913305	19960430
			WO 1996-US6116	19960430
AU 695705	B		AU 1996-56352	19960430
US 5830655	A	CIP of	US 1995-445751	19950522
			US 1996-639363	19960426
JP 11505127	W		JP 1996-535680	19960430
			WO 1996-US6116	19960430
EP 828855	B1		EP 1996-913305	19960430
			WO 1996-US6116	19960430
DE 69605669	E		DE 1996-605669	19960430
			EP 1996-913305	19960430
			WO 1996-US6116	19960430
KR 99021950	A		WO 1996-US6116	19960430
			KR 1997-708425	19971121
CN 1191575	A		CN 1996-195707	19960430
CA 2220418	C		CA 1996-2220418	19960430
			WO 1996-US6116	19960430
JP 3437184	B2		JP 1996-535680	19960430
			WO 1996-US6116	19960430

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9656352	A	Based on	WO 9637630
EP 828855	A1	Based on	WO 9637630
AU 695705	B	Previous Publ.	AU 9656352
		Based on	WO 9637630
JP 11505127	W	Based on	WO 9637630
EP 828855	B1	Based on	WO 9637630

DE 69605669	E	Based on	EP 828855
		Based on	WO 9637630
KR 99021950	A	Based on	WO 9637630
CA 2220418	C	Based on	WO 9637630
JP 3437184	B2	Previous Publ.	JP 11505127
		Based on	WO 9637630

PRIORITY APPLN. INFO: **US 1996-639363 19960426; US 1995-445751 19950522**

AB WO 9637630 A UPAB: 19970108
A novel method (A) for determining the size of a primer extension prod. (PEP), comprises: (a) hybridising a **primer** (P) with a target **nucleic** acid (NA), where the **primer**: (i) is complementary to the target NA; (ii) has a first region containing the 5' end of the primer; and (iii) has a second region containing the 3' end of the primer which is capable of serving as a priming site for enzymatic extension and contains a **cleavable** site; (b) extending the primer enzymatically to generate a mixture containing a prod. composed of the primer and an extension segment; (c) **cleaving** at the **cleavable** site to release the extension segment; and (d) sizing the extension segment by mass spectrometry, where the length of the extension segment is increased relative to the length of the prod. of (b).
USE - The methods can be used for nucleic acid analysis, eg. for gene mapping and identification, for detecting genetic disorders or for detecting the presence of certain bacteria, viruses, fungi or parasites. The method (Ab) may be used for determining a single base **fingerprint**, especially an adenine **fingerprint**.
ADVANTAGE - The methods can provide large amts. of data in a relatively short period of time.
Dwg.0/16

L68 ANSWER 6 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-617299 [66] WPIX
CROSS REFERENCE: 2001-040475 [05]; 2001-366407 [38]; 2002-048724 [06]
DOC. NO. CPI: C2002-174481
TITLE: Isolating DNA containing fragments nicked by Escherichia coli methyl-directed mismatch repair system employs a modified rolling circle **amplification** procedure which utilizes DNA polymerase III.
DERWENT CLASS: B04 D16
INVENTOR(S): LASKEN, R; WEISSMAN, S
PATENT ASSIGNEE(S): (LASK-I) LASKEN R; (WEIS-I) WEISSMAN S; (MOLE-N) MOLECULAR STAGING INC; (UYYA) UNIV YALE
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002076704	A1	20020620	(200266)*		19
US 6576448	B2	20030610	(200340)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002076704	A1 Provisional	US 1998-100996P	19980918
	Div ex	US 1999-398216	19990917
		US 2001-818927	20010328

US 6576448	B2 Provisional	US 1998-100996P	19980918
	Div ex	US 1999-398216	19990917
		US 2001-818927	20010328

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6576448	B2 Div ex	US 6235502

PRIORITY APPLN. INFO: **US 1998-100996P 19980918**; US 1999-398216 19990917; US 2001-818927 20010328

AB US2002076704 A UPAB: 20030624

NOVELTY - Mismatched DNA containing fragments nicked by MutSLH from two DNA samples are isolated by a modified rolling circle amplification (RCA) method. DNA sample is digested with restriction enzyme, the fragments ligated to Y-shaped adapters forming adapter-fragment constructs which are subjected to nicking by MutSLH proteins and nicked fragments are treated with DNA polymerase(s) to elongate the 3' end.

DETAILED DESCRIPTION - Isolating (M1) mismatched DNA containing fragments nicked by MutSLH (a combination of the three proteins of the Escherichia coli methyl-directed mismatch repair system, collectively called MutSLH) from two DNA samples, comprises:

(a) digesting a first DNA sample with a restriction enzyme to obtain DNA fragments;

(b) ligating Y-shaped adapters to the fragments to obtain fragment-plus-adapter constructs;

(c) repeating the above steps with a second sample;.

(d) methylating the products formed from (c) of the first sample but not the second sample;

(e) mixing the methylated and unmethylated products obtained from the samples, denaturing and reannealing to form hemimethylated heterohybrids;

(f) treating the fragments produced in step (e) with a MutSLH preparation to nick DNA containing mismatches and form a 3'-OH end; and

(g) elongating the 3'-OH end with one or more DNA polymerases.

The method can also be carried out by ligating adapters to DNA fragments to obtain fragment-adapter constructs that have a single-stranded (ss) overhang on the 5'-ends and recessed 3'-ends, where the adapters are blocked with a dideoxynucleotide or other modification that prevents the elongation by a DNA polymerase, carrying out (c)-(e) as above, blocking pre-existing nicks on the fragments with dideoxynucleoside triphosphates or their analogs, treating the fragments with MutSLH preparation to form 3'-OH ends and elongating the 3'-OH ends with a DNA polymerase having strand displacement or nick translation capacity.

INDEPENDENT CLAIMS are also included for the following:

(1) amplifying (M2) DNA using RCA in a manner that results in approximately equimolar amplification of DNA, by amplifying a circle DNA molecule which comprises a stem-and-loop, or a circle DNA molecule containing a universal base, an abasic residue, or other residue that alters the rate of circle replication, where elongation of the circle by a replicating polymerase carrying out the amplification is inhibited;

(2) a method (M3) for using RCA to obtain approximately equimolar amplification of DNA fragment mixtures by introducing one pause site in a DNA circle, comprises:

(a) placing within the circle a stretch of one or more abasic sites, a region of high secondary structure and a ligand binding site, and carrying out RCA under conditions such that the pause site slows the DNA

polymerase replicating the circle and tends to equalize the number of times the polymerase copies circles of different length; or

(b) circularizing double stranded DNA (dsDNA) fragments around an adapter such that one strand of the adapter has an internal pause and the outer strand is blocked from ligation at one or both ends; or

(c) using a splint that has an internal double stranded (ds) segment containing a pause site on one DNA strand, and which has single stranded extensions at both ends complementary to the ends of the single-stranded fragment to be amplified;

(3) a method (M4) in which fragments of DNA may be circularized and amplified, by cutting DNA with a restriction enzyme that produces a single fragment containing all the markers of the region having pause to be determined, or using the RecA-assisted restriction endonuclease (RARE) method or its variants to produce such a fragment, ligating the cut DNA around an adapter and amplifying the fragment using RCA to obtain a single stranded DNA (ssDNA) from the desired fragment;

(4) amplifying (M5) segments of a DNA target by RCA, by annealing a padlock DNA that creates a gap comprising the sequence to be amplified, extending the 3'-OH of the padlock DNA with a DNA polymerase which generates a nick, ligating the nick to form a circle **DNA**, annealing an RCA **primer** to the circle **DNA** and carrying out RCA with DNA polymerase III;

(5) a method (M6) in which large fragments of DNA may be circularized and amplified, by providing a DNA-adapter construct which has a DNA fragment ligated around an adapter that has an internal gap and 5' region of non-complementarity and amplifying the DNA-adapter construct using DNA pol III in a RCA;

(6) a method (M7) of ligating adapters onto ends of DNA fragments for use in RCA of the DNA, by ligating restriction endonuclease fragments with an oligonucleotide adapter that forms a hairpin structure with itself such that 3' and 5' ends of the adapter are annealed together and form a proper overhang or blunt end for ligation to the restriction endonuclease fragments, where a circular construct is formed, annealing an **oligonucleotide primer** to the single-stranded loop portion of the adapters and extending the **oligonucleotide primer** with a **DNA** polymerase in RCA reaction; and

(7) a method of carrying out RCA reaction, where at least two different DNA polymerases are employed, one or more of which contains a 3' to 5' exonuclease activity capable of correcting nucleotide misincorporations.

USE - (M1) is useful for isolating mismatched DNA containing fragments nicked by MutSLH from two DNA samples. The procedure is useful for polymorphism analysis (claimed).

The procedure allows for the MutSLH nicking of DNA fragments containing mismatched bases to analyze polymorphism between DNA samples. The methods are useful in phase determination, polymorphism analyses, mismatch scanning procedures and cloning procedures, diagnostics, genotyping, genomic **mapping**, DNA sequencing and synthesis of DNA probes.

ADVANTAGE - DNA polymerase III holoenzyme provides a superior rate of DNA synthesis and also high processivity which allows rapid replication through regions of high GC content, hair-pin structures, and other regions of secondary structure and regions that normally slow replication due to local sequence context effects.

Dwg.0/5

ABEX UPTX: 20021014

EXAMPLE - This example demonstrates the product formed using the DNA polymerase III holoenzyme and primed M13 single-stranded (ss) DNA as the template. The product strands were larger than 12 kb. To prove that the

product DNA consisted of tandem repeats of the M13 sequence, as predicted for a rolling circle amplification (RCA) reaction, the reaction products were digested with EcoRI which converted the product DNA to unit lengths of 7250 kb. RCA assays were in 50 microlitres of reaction buffer (HEPES (4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic acid)-NaOH (pH 7.4), MgCl2 (12 mM), Dithiothreitol (DTT) (5 mM), bovine serum albumin (BSA)/ml (100 mug), ATP (5 mM), glycerol (20%) (v/v)) containing M13mp19 (+) (325 ng) (138 fmol) ssDNA as template, F4 primer: 5'-TCTGTTTATAGGGCCTCTTCGCTATTACGC CAGC-3' (2.5 pmol), PolIII (1 pmol), DnaB (5.5 pmol), DnaG (15.4 pmol), SSB (single-stranded DNA binding protein) (54.2 pmol), ATP, UTP, GTP and CTP (each 50 nM), dATP, dTTP, dGTP and alpha32P-CTP (each 400 microMolar). An aliquot of amplification products was quantitated by spotting onto DE81 filters. After washing and drying, the filters were counted in a liquid scintillation counter. Another aliquot (2 microlitres) was digested with EcoRI or incubated with only EcoRI buffer at 37 degrees Centigrade for 1 hour. The digestion mix was treated with Protease K for 30 minute and then analyzed on a 0.7% alkaline gel followed by exposing to storage Phosphor screen and quantitated.

L68 ANSWER 7 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-048724 [06] WPIX
CROSS REFERENCE: 2001-040475 [05]; 2001-366407 [38]; 2002-617299 [66]
DOC. NO. CPI: C2002-013582
TITLE: Isolating DNA containing fragments nicked by Escherichia coli methyl-directed mismatch repair system involves using a modified rolling circle **amplification** procedure which employs DNA polymerase III.
DERWENT CLASS: B04 D16
INVENTOR(S): LASKEN, R; WEISSMAN, S
PATENT ASSIGNEE(S): (LASK-I) LASKEN R; (WEIS-I) WEISSMAN S
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2001039039	A1	20011108	(200206)*		19

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2001039039	A1 Provisional	US 1998-100996P	19980918
	Div ex	US 1999-398216	19990917
		US 2001-820356	20010329

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2001039039	A1 Div ex	US 6235502

PRIORITY APPLN. INFO: **US 1998-100996P 19980918**; US 1999-398216 19990917; US 2001-820356 20010329
AB US2001039039 A UPAB: 20021018
NOVELTY - Mismatched DNA containing fragments nicked by MutSLH from two DNA samples are isolated by a modified rolling circle amplification (RCA) method. DNA sample is digested with restriction enzyme, the fragments are

ligated to Y-shaped adapters forming adapter-fragment constructs which are nicked by MutSLH proteins and nicked fragments are treated with DNA polymerase(s) which elongates the 3'-OH end.

DETAILED DESCRIPTION - Isolating (M1) mismatched DNA containing fragments nicked by MutSLH (a combination of the three proteins of the Escherichia coli methyl-directed mismatch repair system, collectively called MutSLH) from two DNA samples, comprises:

(a) digesting a first DNA sample with a restriction enzyme to obtain DNA fragments;

(b) ligating Y-shaped adapters to the fragments to obtain fragment-plus-adapter constructs;

(c) repeating the above steps with a second sample;

(d) methylating the products formed from (c) of the first sample but not the second sample;

(e) mixing the methylated and unmethylated products obtained from the samples, denaturing and reannealing to form hemimethylated heterohybrids;

(f) treating the fragments produced in step (e) with a MutSLH preparation to nick DNA containing mismatches and form a 3'-OH end; and

(g) elongating the 3'-OH end with one or more DNA polymerases.

The method can also be carried out by ligating adapters to DNA fragments to obtain fragment-adapter constructs that have a single-stranded (ss) overhang on the 5'-ends and recessed 3'-ends, where the adapters are blocked with a dideoxynucleotide or other modification that prevents the elongation by a DNA polymerase, carrying out (c)-(e) as above, blocking pre-existing nicks on the fragments with dideoxynucleoside triphosphates or their analogs, treating the fragments with MutSLH preparation to form 3'-OH ends and elongating the ends with a DNA polymerase having strand displacement or nick translation capacity.

INDEPENDENT CLAIMS are also included for the following:

(1) amplifying (M2) DNA using RCA in a manner that results in approximately equimolar amplification of the DNA, by amplifying a circle DNA molecule which comprises a stem-and-loop, or a circle DNA molecule containing a universal base, an abasic residue, or other residue that alters the rate of circle replication, where elongation of the circle by a replicating polymerase carrying out the amplification is inhibited;

(2) a method (M3) for using RCA to obtain approximately equimolar amplification of DNA fragment mixtures by introducing at least one pause site in a DNA circle, comprises: (a) placing within the circle a stretch of one or more abasic sites, a region of high secondary structure and a ligand binding site, and then carrying out RCA under conditions such that the pause site slows the DNA polymerase replicating the circle and tends to equalize the number of times the polymerase copies circles of different length; (b) circularizing dsDNA fragments around an adapter such that one strand of the adapter has an internal pause and the outer strand is blocked from ligation at one or both ends; or (c) using a splint that has an internal double stranded (ds) segment containing a pause site on one DNA strand, and which has single stranded extensions at both ends complementary to the ends of the single-stranded fragment to be amplified;

(3) a method (M4) in which fragments of DNA may be circularized and amplified, by cutting DNA with a restriction enzyme that produces a single fragment containing all the markers of the region having pause to be determined, or using the RecA-assisted restriction endonuclease (RARE) method or its variants to produce such a fragment, ligating the cut DNA around an adapter and amplifying the fragment using RCA to obtain a ssDNA from the desired fragment;

(4) amplifying (M5) segments of a DNA target by RCA, by annealing a padlock DNA that creates a gap comprising the sequence to be amplified, extending the 3'-OH of the padlock DNA with a DNA polymerase which generates a nick, ligating the nick to form a circle **DNA**,

annealing an RCA **primer** to the circle **DNA** and carrying out RCA with DNA polymerase III;

(5) a method (M6) in which large fragments of DNA may be circularized and amplified, by providing a DNA-adapter construct which has a DNA fragment ligated around an adapter that has an internal gap and 5' region of non-complementarity and amplifying the DNA-adapter construct using DNA pol III in a RCA;

(6) ligating (M7) adapters onto ends of DNA fragments for use in RCA of the DNA, by ligating restriction endonuclease fragments with an oligonucleotide adapter that forms a hairpin structure with itself such that 3' and 5' ends of the adapter are annealed together and form a proper overhang or blunt end for ligation to the restriction endonuclease fragments, where a circular construct is formed, annealing an **oligonucleotide primer** to the single-stranded loop portion of the adapters and extending the **oligonucleotide primer** with a **DNA** polymerase in RCA reaction; and

(7) carrying out RCA reaction, where at least two different DNA polymerases are employed, one or more of which contains a 3' to 5' exonuclease activity capable of correcting nucleotide misincorporations.

USE - (M1) is useful for isolating mismatched DNA containing fragments nicked by MutSLH from two DNA samples. The procedure allows for the MutSLH nicking of DNA fragments containing mismatched bases to analyze polymorphism between DNA samples. The methods are useful in phase determination, polymorphism analyses, mismatch scanning procedures and cloning procedures, diagnostics (claimed), genotyping, genomic **mapping**, DNA sequencing and synthesis of DNA probes.

ADVANTAGE - DNA polymerase III holoenzyme provides a superior rate of DNA synthesis and also high processivity which allows rapid replication through regions of high GC content, hair-pin structures, and other regions of secondary structure and regions that normally slow replication due to local sequence context effects.

DESCRIPTION OF DRAWING(S) - The figure shows the fragment plus adapter constructs obtained by ligating adapters to DNA fragments, in the amplification of specific DNA sequences by rolling circle amplification. Dwg.1A/5

ABEX UPTX: 20020128

EXAMPLE - This example demonstrates the product formed using the DNA polymerase III holoenzyme and primed M13 single-stranded (ss) DNA as the template. The product strands were larger than 12 kb. To prove that the product DNA consisted of tandem repeats of the M13 sequence, as predicted for a rolling circle amplification (RCA) reaction, the reaction products were digested with EcoRI which converted the product DNA to unit lengths of 7250 kb. RCA assays were in 50 mul of reaction buffer (HEPES (4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic acid)-NaOH (pH 7.4), MgCl2 (12 mM), Dithiothreitol (DTT) (5 mM), bovine serum albumin (BSA)/ml (100 mug), ATP (5 mM), glycerol (20%) (v/v)) containing M13mp19 (+) (325 ng) (138 fmol) ssDNA as template, F4 primer: 5'-TCTGTTTATAGGGCCTCTTCGCTATTACGC CAGC-3' (2.5 pmol), PolIII (1 pmol), DnaB (5.5 pmol), DnaG (15.4 pmol), SSB (single-stranded DNA binding protein) (54.2 pmol), ATP, UTP, GTP and CTP (each 50 nM), dATP, dTTP, dGTP and alpha32P-CTP (each 400 muM). An aliquot of amplification products was quantitated by spotting onto DE81 filters. After washing and drying, the filters were counted in a liquid scintillation counter. Another aliquot (2 mul) was digested with EcoRI or incubated with only EcoRI buffer at 37degreesC for 1 hour. The digestion mix was treated with Protease K for 30 minute and then analyzed on a 0.7% alkaline gel followed by exposing to storage Phosphor screen and quantitated.

L68 ANSWER 8 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-540404 [60] WPIX
CROSS REFERENCE: 1994-249246 [30]; 1994-317040 [39]; 1996-392630 [39]; 1996-443204 [44]; 1997-503121 [46]; 1998-017627 [02]; 1998-286850 [25]; 1998-286851 [25]; 1998-286975 [25]; 2000-270337 [23]; 2001-256361 [26]; 2001-315576 [33]; 2001-327240 [34]; 2001-366403 [38]; 2001-450360 [48]; 2001-482100 [52]; 2001-624663 [72]; 2002-224109 [28]; 2003-895272 [82]
DOC. NO. CPI: C2001-161264
TITLE: Detecting target nucleic acid sequence in sample, useful for diagnosing genetic disease or chromosomal abnormality, comprises amplifying nucleic acid containing target sequence and detecting amplified product by mass spectrometry.
DERWENT CLASS: B04 D16
INVENTOR(S): KOESTER, H
PATENT ASSIGNEE(S): (SEQU-N) SEQUENOM INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6277573	B1	20010821	(200160)*		92

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6277573	B1 CIP of	US 1995-406199	19950317
	Cont of	US 1996-617256	19960318
		US 1999-287681	19990406

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6277573	B1 CIP of	US 5605798
	Cont of	US 6043031

PRIORITY APPLN. INFO: **US 1996-617256 19960318; US 1995-406199 19950317;** US 1999-287681 19990406

AB US 6277573 B UPAB: 20031223
NOVELTY - Detecting (M) target nucleic acid sequence(s) (T) in a biological sample, comprising performing on nucleic acid molecule(s) (NA) containing (T), a first polymerase chain reaction to produce a first amplification product (P1), performing on P1, a second PCR to produce a second amplification product (P2), and detecting P2 by mass spectrometry, thus detecting the presence of (T) in the biological sample, is new.

DETAILED DESCRIPTION - (M) comprising performing a first PCR containing a first forward and reverse primer, which can amplify a portion of NA comprising a portion of (T), thus producing P1, performing on P1, a second PCR comprising a second forward primer and reverse primer, which can amplify a portion of P1 comprising a portion of (T), thus producing P2 and detecting P2 by mass spectrometry, is new.

USE - (M) is useful for detecting the presence of target nucleic acid sequence(s) in a biological sample obtained from an individual, and detecting (T) provides DNA **fingerprint** or is indicative of a

disease or condition such as genetic disease, chromosomal abnormality, genetic predisposition, viral infection, fungal infection, bacterial infection, and protist infection (claimed). (M) is useful to diagnose (e.g., prenatally or postnatally) a genetic disease or chromosomal abnormality, a predisposition to a disease or condition (e.g., obesity, atherosclerosis, cancer), or infection by a pathogenic organism (e.g. virus, bacteria, parasitic or fungus), or to provide information relating to identity heredity, or compatibility (e.g. human leukocyte antigen (HLA) phenotyping).

ADVANTAGE - (M) is fast, highly accurate and reliable for detecting NA and sequences in the molecules.

Dwg.0/48

ABEX UPTX: 20011018

EXAMPLE - Detection of the cystic fibrosis mutation, DELTAF508 by single step dideoxy extension and analysis by matrix assisted laser ionization-time of flight (MALDI-TOF) mass spectrometry was as follows. Amplification was carried out with exon 10 specific primers using standard polymerase chain reaction (PCR) conditions. The reverse primer was 5' labeled with biotin and column purified. After amplification the PCR products were purified by column separation and immobilized on streptavidin coated magnetic beads. DNA was denatured and washed to remove the non-biotinylated sense strand. The beads containing ligated antisense strand were resuspended in 18 micro liter of a reaction mix (2 micro liter 10x Taq buffer, 1 micro liter (1 unit) Taq polymerase, 2 micro liter of 2 mM dGTP, and 13 micro liter H2O) and incubated at 80 degrees C for 5' before the addition of reaction mix 2 (100 ng each of competitive oligonucleotide single base extension (COSBE) primers). The temperature was reduced to 60 degrees C and the mixtures incubated for 5' annealing/extension period. The beads were then washed in 25 mM triethylammonium acetate (TEAA) followed by 50 mM ammonium citrate. The primers were Ex 10 PCR (forward): 5'-Bio-GCAAGTGAATCCTGAGCGTG-3', Ex 10 PCR (reverse): 5'-GTGTGAAGGGTTCATATGC-3', COSBE DELTAF508-N 5'-ATCTATATTCATCATAGGAAACACCACA-3' (28-mer), and COSBE DELTAF508-M 5'-GTATCTATATTCATCATAGGAAACACCATT-3' (30-mer). After washing, beads were resuspended in 1 micro liter 18 Mohm cm H2O. 300 nL each of matrix solution and resuspended beads were mixed on a sample target and allowed to dry. Up to 20 samples were spotted on a probe target disk for introduction into the source region of an unmodified thermo bioanalysis visions 2000 MALDI-TOF operated in reflectron mode with 5 and 20 kV on the target and conversion dynode, respectively. Theoretical average molecular weights (Mr(calc)) were calculated from atomic compositions. Vendor provided software was used to determined peak centroids using external calibration. 1.08 Dalton (Da) was subtracted from these to correct for the charge carrying proton mass to yield the test Mr(exp) values. Upon annealing to the bound template, the N and M primers were presented with dGTP, only primers with proper Watson-Crick base paring at the variable (V) position were extended by the polymerase. If V paired with 3'-terminal base of N, N was extended to a 8837.9 Da product (N+1). If V was properly matched to the M terminus, M was extended to a 9477.3 Da M+1 product.

L68 ANSWER 9 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-450361 [48] WPIX
CROSS REFERENCE: 2000-206023 [18]
DOC. NO. CPI: C2001-135958
TITLE: Analyzing a polynucleotide produced by amplifying cDNA or genomic DNA involves hybridizing terminus probes having constant and variable region to adapter-modified restriction fragment generated from the polynucleotide.
DERWENT CLASS: B04 D16

INVENTOR(S): HUNKAPILLER, M W; RICHARDS, J H
PATENT ASSIGNEE(S): (PEKE) PERKIN-ELMER CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6258539	B1	20010710	(200148)*		19

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6258539	B1 CIP of	US 1998-135381	19980817
		US 1999-303774	19990430

PRIORITY APPLN. INFO: US 1999-303774 19990430;
US 1998-135381
19980817

AB US 6258539 B UPAB: 20010829
NOVELTY - Analyzing a polynucleotide by forming restriction fragment (RF) having first, second terminus and a termini generated by restriction endonuclease (RE), from the polynucleotide, joining an adapter to a terminus of RF to produce adapter-modified RF (I) and hybridizing a terminus probe having constant and variable region to single strand of (I) at a position including the terminus generated by RE.

USE - Analyzing a polynucleotide which is a cDNA or genomic DNA, or which is produced by amplifying a portion of a cDNA preparation or a portion of genomic DNA preparation (claimed).

The method allows simultaneous analysis of multiple different polynucleotides of polynucleotide composition e.g., cDNA or genomic DNA libraries, and the isolation of polynucleotides of interest identified through the analytical techniques. The analysis of RNA populations has utilities in research, diagnosis or treatment of a variety of diseases. The base sequence information contained within identifier sequences can be used to detect, discover or compare polymorphic sequences, to develop **oligonucleotide primers** to isolate the polynucleotide from which a specific identifier sequence is derived.

Analysis of large complex populations of polynucleotides may be used to produce sufficient information about a polynucleotide population so that differences between polynucleotide populations may be ascertained. Thus **fingerprints** of a polynucleotide population may be compared with **fingerprints** of other complex polynucleotide populations.

ADVANTAGE - The method permits the simultaneous analysis of a large number of different mRNA molecules that form a given mRNA population. Multiple identifier sequences may be obtained in parallel, thus permitting the rapid characterization of the large number of polynucleotides.

DESCRIPTION OF DRAWING(S) - The figure shows the terminus probes which hybridize to adapter-modified representative restriction fragments.
Dwg.1A/7

ABEX UPTX: 20010829
WIDER DISCLOSURE - The following are also disclosed:
(1) oligonucleotide arrays having a set of oligonucleotide features, where the oligonucleotides of each feature has a constant and a variable region; and
(2) kits for performing the polynucleotide analysis.

EXAMPLE - None given.

L68 ANSWER 10 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-450360 [48] WPIX
CROSS REFERENCE: 1994-249246 [30]; 1994-317040 [39]; 1996-392630 [39]; 1996-443204 [44]; 1997-503121 [46]; 1998-017627 [02]; 1998-286850 [25]; 1998-286851 [25]; 1998-286975 [25]; 2000-270337 [23]; 2001-256361 [26]; 2001-315576 [33]; 2001-327240 [34]; 2001-366403 [38]; 2001-482100 [52]; 2001-540404 [60]; 2001-624663 [72]; 2002-224109 [28]; 2003-786994 [74]; 2003-895272 [82]
DOC. NO. CPI: C2001-135957
TITLE: Use of mass spectrometry for identifying or detecting target nucleotide(s) present in nucleic acid molecule(s).
DERWENT CLASS: B04 D16
INVENTOR(S): BRAUN, A; KOESTER, H; LITTLE, D P
PATENT ASSIGNEE(S): (SEQU-N) SEQUENOM INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6258538	B1	20010710	(200148)*		95

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6258538	B1	CIP of	US 1995-406199	19950317
		Cont of	US 1996-617256	19960318
		Cont of	US 1999-287679	19990406
			US 1999-287679	19990406

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6258538	B1	CIP of	US 5605798
		Cont of	US 6043031

PRIORITY APPLN. INFO: **US 1996-617256 19960318; US 1995-406199 19950317;** US 1999-287679 19990406

AB US 6258538 B UPAB: 20031223
NOVELTY - Use of mass spectrometry for identifying target nucleotide(s) present in nucleic acid molecule(s), detecting a target nucleotide present in a biological sample and determining whether a target nucleotide present in nucleic acid molecule(s), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) identifying (M1) a target nucleotide (T) present in a nucleic acid molecule (N) involves:

(a) obtaining (N) that contains (T);

(b) optionally immobilizing (N) onto a solid support, to produce an immobilized (N); hybridizing (N) with (P) oligonucleotide that is complementary to (N) at a site adjacent to (T);

(c) contacting the product with a complete set (I) of dideoxynucleoside triphosphates (ddNTP) or 3'-deoxynucleoside triphosphates (3'-dNTP), and a polymerase, so that only the

dideoxynucleoside or 3'-dNTP that is complementary to (T) is extended onto (P);

(d) ionizing or volatilizing the product and determining the molecular mass of the extended (P) by mass spectrometry, thus identifying (T);

(2) identifying (M2) (T)s present in several (N) involves:

(a) hybridizing several (N) with (P) that are complementary to a site immediately adjacent to (T), where a (P) that hybridizes to one of the several (N) or its extension product, is distinguishable from each (P) or its extension product that hybridizes to a different (N), thereby producing one or more hybridized (P)s;

(b) contacting the hybridized (P)s with (I) and a DNA dependent polymerase, so that only a ddNTP or 3'-dNTP that is complementary to (T) is extended onto a hybridized (P); and

(c) determining the molecular masses of the products by mass spectrometry, thereby identifying (T) present in the several (N);

(3) detecting (M3) (T) present in a biological sample, involves:

(a) obtaining (N) that contains (T);

(b) hybridizing (N) with (P) that is complementary to (N) at a site adjacent to (T);

(c) contacting the product with ddNTP or a 3'-dNTP, and a DNA polymerase, whereby if the ddNTP or 3'-dNTP is complementary to (T), it is extended onto (P);

(d) ionizing and volatilizing the product and detecting the (P) by mass spectrometry, to determine the identity of (T);

(4) determining (M4) whether (T) is present in (N) involves:

(a) hybridizing (N) to (P), which is complementary to a sequence of target (N), which is adjacent to the region suspected to contain (T), thereby producing a hybridized (P);

(b) contacting the hybridized (P) with:

(i) three dNTPs;

(ii) a chain terminating nucleotide such as a ddNTP or a 3'-dNTP, where the chain terminating nucleotide corresponds to the missing dNTP; and

(iii) DNA polymerase whereby the hybridized (P) is extended until a chain terminating nucleotide is incorporated to produce an extended (P); and

(c) determining the molecular mass of the extended (P) by mass spectrometry, thereby determining whether (T) is present in (N);

(5) determining (M5) whether (T) is present in several (N), involves:

(a) hybridizing each (N) with (P), which is complementary to a sequence of (N) that is adjacent to a region suspected of containing (T), where a (P) that hybridizes to one (N) of the several (N), is distinguishable from each (P) that hybridizes to a different (N) in the set of (N), thereby producing hybridized (P)s;

(b) contacting the hybridized (P)s with:

(i) three dNTPs and a chain terminating nucleotide such as a ddNTP or a 3'-dNTP (where the chain terminating nucleotide corresponds to the missing dNTP); and

(ii) a DNA polymerase, whereby the hybridized (P)s extended until a chain terminating nucleotide is incorporated, thereby producing extended (P)s; and

(c) determining the molecular masses of the extended (P)s by mass spectrometry, thereby determining whether (T) is present in (N) among the several (N).

USE - Identifying target nucleotide(s) present in a DNA or RNA molecule(s), detecting a target nucleotide present in a biological sample and determining whether a target nucleotide present in nucleic acid molecule(s). The target nucleotides are identified, detected, determined

in nucleic acid molecule(s) obtained from an individual, and where the target nucleotide(s) provides a DNA fingerprint or is indicative of a genetic disease, chromosomal abnormality, a genetic predisposition, a fungal infection, a bacterial infection or a protist infection. The presence of the target nucleotide also indicates the presence of a mutation (claimed).

The target nucleotide(s) detected provide a DNA fingerprint or is indicative of a genetic disease, chromosomal abnormality (either prenatally or postnatally), a genetic predisposition to a disease or condition (such as obesity, atherosclerosis, cancer), a fungal infection, a bacterial infection or a protist infection. The presence of the target nucleotide also indicates the presence of a mutation. They also provide information relating to identity, heredity, or compatibility (human leukocyte antigen (HLA) genotyping).

The method is suitable for the detection of single point mutations or microlesions of DNA and is also applicable in each disease gene or polymorphic region in the genome-like variable number of tandem repeats (VNTR) or other single nucleotide polymorphisms (e.g., apolipoprotein E gene).

ADVANTAGE - The processes described above provide for increased accuracy, and reliability of nucleic acid detection by mass spectrometry, in addition the processes allow for regress controls to prevent false positive or false negative results.

Also, they are much more reliable than currently available procedures, faster, less expensive, avoid electrophoretic steps, and labeling and subsequent detection of a label.

Dwg.0/48

ABEX UPTX: 20010829

EXAMPLE - The solid-phase oligo base extension method detects point mutations and small deletions as well as small insertions in amplified DNA. The method was based on the extension of a detection primer that anneals adjacent to a variable nucleotide position on an affinity-captured amplified template, using a DNA polymerase, a mixture of three deoxynucleoside triphosphates (dNTPs), and the missing one dideoxynucleotide. The resulting products were evaluated and resolved by matrix-assisted laser desorptions/ionization-time of flight mass spectrometry.

The method used a single detection primer followed by a oligonucleotide extension step to give products, differing in length by some bases specific for mutant or wild type alleles which can be easily resolved by MALDI-TOF mass spectrometry. The method was described using exon 10 of the cystic fibrosis transmembrane conductance regulator (CFTR)-gene. Exon 10 of this gene leads in the homozygous state to the clinical phenotype of cystic fibrosis. Genomic DNA were obtained from healthy individuals, individuals homozygous or heterozygous or heterozygous for the DELTAF508 mutation, and one individual heterozygous for the 1506S mutation.

The primers for polymerase chain reaction (PCR) amplification were CFEx10-F (5-GCAAGTGAATCCTGAGCGTG-3' and CFEx10-R (5'-GTGTGAAGGGCGTG-3'. Amplification products were purified. 10 mul aliquots of the purified PCR product were transferred to one well of a streptavidin-coated microtiter plate. Subsequently, 10 mul incubation buffer (80 mM sodium phosphate, 400 mM NaCl, 0.4% Tween 20, pH 7.5) and 30 mul water were added. After incubation for 1 hour at room temperature the wells were washed.

To denature the double stranded DNA the wells were treated with 100 mul of a 50 mM NaOH solution for 3 minutes and the wells were washed three times with 200 mul washing buffer. The annealing of 25 pmol detection primer 5'-CTATATTCATCATAGGAAACACCA-3' was preformed in 50 mul annealing buffer (20 mM Tris, 10 mM KCl, 10 mM (NH4)2SO4, 2 mM MgSO4, 1% Triton X-100, pH 8.75) at 50degreesC for 10 minutes. The wells were washed. The total

reaction consisting of 21 mul, 6 mul Sequenase (RTM)-buffer, 3 mul 110 mM DTT solution, 4.5 mul, 0.5 mM of three dNTPs, 4.5 mul, 2 mM the missing one ddNTP, 5.5 mul glycerol enzyme dilution buffer, 0.25 mul Sequenase 2.0, and 0.25 pyrophosphatase.
The reaction was pipetted on ice and then incubated. The wells were washed three times with 200 mul washing buffer and once with 60 mul of a 70 mM NH4-Citrate solution. The extended primer was denatured. For precipitation, 10 mul NH4-acetate (pH 6.5),0.5 mul glycon and 100 mul absolute ethanol were added to the supernatant and incubated. After centrifugation the pellet was washed in 70% ethanol and resuspended in 1 mul 18 Mohm/cm H2O. Sample preparation was performed by mixing 0.3 mul of each of matrix solution and of resuspended DNA/glycogen pellet on a sample target and allowed to air dry.
Theoretical average molecular mass (Mr(calc)) were calculated from atomic compositions; reported experimental Mr(Mr(exp)) values were those of the singly-protonated form, determining using external calibration. All samples were confirmed by standard Sanger sequencing which showed no discrepancy in comparison to the mass spec analysis. The accuracy of the experimental measurements of the various molecular masses was within a range of minus 21.8 and plus 87.1 Dalton to the range expected. This was a definitive interpretation of the results allowed in each case.

L68 ANSWER 11 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-373720 [39] WPIX
CROSS REFERENCE: 1999-619652 [53]; 2001-588922 [56]
DOC. NO. CPI: C2001-114126
TITLE: New method for multifragment in vivo cloning using homologous recombination of PCR **amplified** fragments, used particularly for **mapping** phenotypically expressed mutations.
DERWENT CLASS: B04 D16
INVENTOR(S): MARYKWAS, D L; PASSMORE, S E
PATENT ASSIGNEE(S): (MARY-I) MARYKWAS D L; (PASS-I) PASSMORE S E
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6238923	B1	20010529	(200139)*		26

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6238923	B1 Cont of	US 1996-584322	19960113
		US 1999-430911	19991101

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6238923	B1 Cont of	US 5976846

PRIORITY APPLN. INFO: **US 1996-584322 19960113**; US 1999-430911 19991101
AB US 6238923 B UPAB: 20011119
NOVELTY - Directed in vivo DNA recombination resulting in the production of a circular double stranded DNA molecule is new.

DETAILED DESCRIPTION - Directed in vivo DNA recombination resulting in the production of a circular double stranded DNA molecule comprising:

(a) a first container comprising an aliquot of the full length mutant 1 double stranded (ds) DNA amplifying a first ds mutant 1 DNA segment by polymerase chain reaction (PCR). Primers for amplification are provided;

(b) a second container comprises a linear gapped acceptor vector capable of replication and selection in a host with an efficient and precise in vivo homologous recombination system. The vector is linearized with appropriate restriction enzymes;

(c) a first container comprises a full length mutant 2 ds DNA amplifying a first ds mutant 2 **DNA** segment using PCR. Suitable **primers** are provided the primers effect the amplification such that the first ds mutant 1 DNA segment and the first ds mutant 2 segment are homologous within the region to be recombined and where one end of the first ds mutant 1 DNA segment is homologous to an end of a linear gapped acceptor plasmid and where one end of the first ds mutant 2 DNA segment is homologous to the other end of the acceptor vector;

(d) transforming the product of (a) and the product of (b) and (c) together into a host with a suitable efficient and accurate in vivo recombination system allowing the products to recombine in vivo at the homologous sequences producing a collection of recombined double stranded circular DNA molecules.

USE - The method is useful to assemble DNA fragments into plasmids that can replicate in vivo. Such a plasmid is useful to introduce the fragment in to an RNA or DNA vector.

Dwg.0/6

ABEX UPTX: 20010716

EXAMPLE - No example is given.

L68 ANSWER 12 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-422808 [36] WPIX
DOC. NO. NON-CPI: N2000-315540
DOC. NO. CPI: C2000-127847
TITLE: Genotype analysis method, defined as SOMA (short oligonucleotide mass analysis), of short, defined **amplification** products using electro-spray ionization mass spectrometry, useful for analyzing the genotype of living organisms.
DERWENT CLASS: B04 D16 J04 S03 V05
INVENTOR(S): FRIESEN, M D; GROOPMAN, J D; JACKSON, P E; KINZLER, K W; LAKEN, S J; VOGELSTEIN, B
PATENT ASSIGNEE(S): (UYJO) UNIV JOHNS HOPKINS; (FRIE-I) FRIESEN M D; (GROO-I) GROOPMAN J D; (JACK-I) JACKSON P E; (KINZ-I) KINZLER K W; (LAKE-I) LAKEN S J; (VOGE-I) VOGELSTEIN B
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000031300	A2	20000602	(200036)*	EN	40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000017395	A	20000613	(200043)		
EP 1133573	A2	20010919	(200155)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT					

RO SE SI
US 2002102556 A1 20020801 (200253)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000031300	A2	WO 1999-US27523	19991122
AU 2000017395	A	AU 2000-17395	19991122
EP 1133573	A2	EP 1999-960522	19991122
		WO 1999-US27523	19991122
US 2002102556	A1 Div ex	US 1998-198340	19981124
		US 2001-774021	20010131

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000017395	A Based on	WO 2000031300
EP 1133573	A2 Based on	WO 2000031300

PRIORITY APPLN. INFO: **US 1998-198340 19981124**; US 2001-774021 20010131

AB WO 200031300 A UPAB: 20000801
NOVELTY - A method, defined as SOMA (short oligonucleotide mass analysis), of genotype analysis in which short, defined fragments of amplification are produced by simple enzymatic digestion and directly analyzed by electro-spray ionization mass spectrometry (ESI-MS), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) An isolated primer (P1) for amplifying a segment of DNA comprising a linear oligonucleotide comprising a 5' end and a 3' end, the oligonucleotide consisting of at least 35 nucleotides, where a first portion of at least 13 nucleotides at the 5' end and a second portion of 5 to 22 nucleotides at the 3' end are precisely or substantially complementary to a first portion and a second portion, respectively, of a segment of a cDNA or genomic DNA, where 4-8 nucleotides between the first portion and the second portion of the oligonucleotide comprise a recognition site for a restriction endonuclease that **cleaves** at least 5 nucleotides from its recognition site, while the segment of the cDNA or genomic DNA does not comprise the recognition site;

(2) A primer pair (P2) where each primer is:
(a) P1;

(b) complementary to an opposite strand of a double stranded cDNA or genomic DNA molecule; and

(c) complementary to two non-contiguous portions of the double stranded cDNA or genomic DNA molecule, where 1 to 20 nucleotides separate the two non-contiguous portions of the double stranded cDNA or genomic DNA molecule;

(3) a kit comprising P2;

(4) A method for producing a short segment of DNA, suitable for analysis by mass spectrometry, comprising:

(a) amplifying cDNA or genomic DNA of a subject using P2 to form amplified DNA;

(b) digesting the amplified DNA with the restriction endonuclease to form a short segment of DNA; and

(5) A method for analyzing a first short segment of DNA having a first polymorphic nucleotide to distinguish it from a second short segment

of DNA having a second polymorphic nucleotide, comprising applying a mixture of DNA segments, produced by the method of (4), to an electrospray ionization/mass spectrometer, where the DNA segments are denatured and separated.

USE - The method is useful for analyzing the genotype of living organisms, including humans, by electrospray ionization mass spectrometry.

ADVANTAGE - The method is simple to implement, extremely accurate and applicable to most DNA variations.

Dwg.0/5

ABEX UPTX: 20000801

EXAMPLE - A second variant in the APC (undefined) gene (ACA or ACG at codon 1493) was selected to demonstrate the general applicability of the SOMA (short oligonucleotide mass analysis) method. This variant is not associated with disease, but is a common polymorphism which can be used for linkage analysis in families with familial adenomatous polyposis. Primers used for polymerase chain reaction (PCR) amplification of the APC variants were:

1493 sense: 5'-TTCAGAGGGTCCAGGTTCTTCCTGGAGCTGATACTTTATTACA-3'; and

1493 antisense: 5'-GCACTCAGGCTGGATGAACAACTGGAGCCATCTGGAGTACT-3'

The expected size of the product was 100 basepairs (bp). The internal fragments generated by SOMA were designed to be 16 bp long. Moreover for one of the alleles (ACG), the sense (5'-TTTTGCCACGGAAAGT-3') and antisense (5'-TTTCCGTGGcAAAATG-3') oligonucleotides had different base sequences but the same mass. This resulted in two oligonucleotide (M-3H)3- ions with identical mass-to-charge ratios at 1657.7 which could not be resolved by electro-spray ionization mass spectrometry (ESI-MS). However, it was found that ESI-MS/MS selected reaction monitoring could easily differentiate between the four oligonucleotide ions. Heterozygotes were identified by the presence of chromatographic peaks in all four channels, while peaks in the sense and antisense channels of one allele indicated a homozygous sample. Of 50 individuals genotyped at codon 1493, there was a 100% correlation between the results obtained by SOMA and sequencing.

L68 ANSWER 13 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-293188 [25] WPIX
CROSS REFERENCE: 2002-362259 [39]
DOC. NO. CPI: C2000-088711
TITLE: **Cleaving** a polynucleotide for detection of variance in nucleotide sequence, full sequence determination of a polynucleotide, genotyping of DNA and labeling a polynucleotide fragment.
DERWENT CLASS: B04 D16
INVENTOR(S): KAWATE, T; STANTON, V P; VERDINE, G; WOLFE, J L; OLSON, J; ZILLMANN, M; VERDINE, G L; ALLERSON, C R; ALLERSON, C
PATENT ASSIGNEE(S): (VARI-N) VARIAGENICS INC; (VARI-N) VARIAGENICS CORP; (KAWA-I) KAWATE T; (STAN-I) STANTON V P; (VERD-I) VERDINE G L; (WOLF-I) WOLFE J L; (OLSO-I) OLSON J; (ALLE-I) ALLERSON C R
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000018967	A1	20000406	(200025)*	EN	290

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT

UA UG UZ VN YU ZW
AU 2000012004 A 20000417 (200035)
NO 2001001607 A 20010531 (200138)
EP 1117838 A1 20010725 (200143) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 9914262 A 20020122 (200216)
KR 2001099663 A 20011109 (200229)
US 6440705 B1 20020827 (200259)
JP 2002525129 W 20020813 (200267) 324
US 6458945 B1 20021001 (200268)
US 2002150943 A1 20021017 (200270)
US 6566059 B1 20030520 (200336)
US 2003087398 A1 20030508 (200337)
US 6582923 B2 20030624 (200343)
US 2003134290 A1 20030717 (200348)
US 6610492 B1 20030826 (200357)
US 2003165880 A1 20030904 (200359)
MX 2001003404 A1 20020301 (200362)
CN 1463292 A 20031224 (200421)
US 6777188 B2 20040817 (200454)
AU 774388 B2 20040624 (200468)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000018967	A1		WO 1999-US22988	19990930
AU 2000012004	A		AU 2000-12004	19990930
NO 2001001607	A		WO 1999-US22988	19990930
			NO 2001-1607	20010329
EP 1117838	A1		EP 1999-969748	19990930
			WO 1999-US22988	19990930
BR 9914262	A		BR 1999-14262	19990930
			WO 1999-US22988	19990930
KR 2001099663	A		KR 2001-704172	20010331
US 6440705	B1	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817
			US 1999-394457	19990910
JP 2002525129	W		WO 1999-US22988	19990930
			JP 2000-572414	19990930
US 6458945	B1	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817
		Div ex	US 1999-394774	19990910
			US 2000-709596	20001109
US 2002150943	A1	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817
		CIP of	US 1999-394467	19990910
			US 2002-107751	20020326
US 6566059	B1	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817
			US 1999-394467	19990910
US 2003087398	A1	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817
		Div ex	US 1999-394774	19990910
		Div ex	US 2000-709596	20001109
			US 2002-104818	20020322
US 6582923	B2	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817

		Div ex	US 1999-394774	19990910
		Div ex	US 2000-709596	20001109
			US 2002-104818	20020322
US 2003134290	A1	Provisional	US 1998-102724P	19981001
		CIP of	US 1999-394387	19990910
		CIP of	US 1999-394457	19990910
		CIP of	US 1999-394467	19990910
		CIP of	US 1999-394774	19990910
		Div ex	US 2000-655104	20000905
			US 2002-105101	20020322
US 6610492	B1	Provisional	US 1998-102724P	19981001
		CIP of	US 1999-394467	19990910
			US 2002-43511	20020108
US 2003165880	A1	Provisional	US 1998-102724P	19981001
		CIP of	US 1999-394467	19990910
			US 2002-107748	20020326
MX 2001003404	A1		WO 1999-US22988	19990930
			MX 2001-3404	20010402
CN 1463292	A		CN 1999-813928	19990930
US 6777188	B2	Provisional	US 1998-102724P	19981001
		Provisional	US 1999-149533P	19990817
		CIP of	US 1999-394467	19990910
			US 2002-107751	20020326
AU 774388	B2		AU 2000-12004	19990930

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000012004	A	Based on	WO 2000018967
EP 1117838	A1	Based on	WO 2000018967
BR 9914262	A	Based on	WO 2000018967
JP 2002525129	W	Based on	WO 2000018967
US 6582923	B2	Div ex	US 6458945
US 2003134290	A1	CIP of	US 6440705
US 2003165880	A1	CIP of	US 6566059
MX 2001003404	A1	Based on	WO 2000018967
US 6777188	B2	CIP of	US 6566059
AU 774388	B2	Previous Publ.	AU 2000012004
		Based on	WO 2000018967

PRIORITY APPLN. INFO: US 1999-394774 19990910;
US 1998-102724P
19981001; US 1999-149533P
19990817; US 1999-394387
19990910; US 1999-394457
19990910; US 1999-394467
19990910; US 2000-709596
20001109; US 2002-107751
20020326; US 2002-104818
20020322; US 2000-655104
20000905; US 2002-105101
20020322; US 2002-43511
20020108; US 2002-107748
20020326

AB WO 200018967 A UPAB: 20041026
NOVELTY - **Cleaving** a polynucleotide comprising replacing one or more natural nucleotides at each point occurrence with modified nucleotides and contacting the modified polynucleotide with a reagent that

cleaves the polynucleotide at each point occurence, is new.

DETAILED DESCRIPTION - A method (M1) for **cleaving** a polynucleotide comprises:

(a) replacing one or more natural nucleotides at each point occurrence in a polynucleotide with modified nucleotides to form a modified polynucleotide providing, when only one natural nucleotide is being replaced, the modified nucleotide is not a ribonucleotide or a nucleoside alpha -thiotriphosphate; and

(b) contacting the modified polynucleotide with a reagent(s) that **cleaves** the modified polynucleotide at each point occurrence of the one or more modified nucleotides.

INDEPENDENT CLAIMS are also included for the following:

(1) a method (M2) for determining nucleotide sequence in a polynucleotide comprising:

(a) replacing a natural nucleotide at a percentage of points of occurrence in a polynucleotide with a modified nucleotide to form a modified polynucleotide where the modified polynucleotide is not a ribonucleotide;

(b) **cleaving** the modified polynucleotide into fragments at substantially each point of occurrence of the modified nucleotide;

(c) repeating steps (a) and (b), each time replacing a different natural nucleotide with a modified nucleotide; and either

(d) determining the masses of the fragments obtained from each **cleavage** reactions and constructing the sequence of the polynucleotide from the masses; or

(e) **analyzing** a **sequence** ladder obtained from the fragments in step (c);

(2) a method (M3) for determining nucleotide sequence in a polynucleotide comprising:

(a) replacing a first natural nucleotide at a percentage of points of incorporation in a polynucleotide with a first modified nucleotide, where the first modified nucleotide is not a ribonucleotide or a nucleoside alpha -thiophosphate, to form a first partially modified polynucleotide;

(b) **cleaving** the first partially modified nucleotide into fragments using the **cleaving** procedure of known **cleavage** efficiency to form a first set of nucleotide specific **cleavage** products;

(c) repeating steps (a) and (b) replacing a second, a third and a fourth natural nucleotide with a second, third and fourth modified nucleotide to form a second, third and fourth partially modified polynucleotide which, upon **cleavage**, afford a second, third and fourth set of nucleotide specific **cleavage** products;

(d) performing gel electrophoresis on the first, second, third and fourth set of nucleotide specific **cleavage** products to form a sequence ladder; and

(e) reading the sequence of the polynucleotide from the sequence ladder;

(3) a method (M4) for **cleaving** a polynucleotide during polymerization›comprising:

(a) mixing together four different nucleotides, one or two of which are modified nucleotides; and

(b) two or more polymerases, at least one of which produces or enhances **cleavage** at points where the modified nucleotide is being incorporated or, if two modified nucleotides are used, at points where one of the modified nucleotides is followed immediately in sequence by the other modified nucleotide;

(4) a method (M5) for **cleaving** a polynucleotide such that all fragments obtained from the **cleavage** carry a label comprising:

(a) replacing a natural nucleotide partially or at each point of occurrence in a polynucleotide with a modified nucleotide to form a modified polynucleotide; and

(b) contacting, in the presence of a phosphine covalently bonded to a label, the modified polynucleotide with a reagent(s) which **cleave** (s) the modified polynucleotide partially or at each point of occurrence;

(5) a method (M6) for detecting a variance in nucleotide sequence in a polynucleotide, for sequencing a polynucleotide or for genotyping a polynucleotide known to contain a polymorphism or mutation comprising:

(a) replacing one or more natural nucleotides in the polynucleotide with one or more modified nucleotides where the modification is selected from a modified base, a modified sugar and a modified phosphate ester, providing that if only one natural nucleotide is being replaced the modified nucleotide is not a ribonucleotide or a nucleoside alpha -thiotriphosphate;

(b) contacting the modified polynucleotide with a reagent(s) which **cleave** the modified polynucleotide into fragments at sites of incorporation of the modified nucleotide; and

(c) analyzing the fragments to detect the variance to construct the sequence or to genotype the polynucleotide;

(6) a mutant polymerase which is capable of catalyzing the incorporation of a modified nucleotide into a polynucleotide where the modified nucleotide is not a ribonucleotide obtained by a process comprising DNA shuffling, cell senescence selection or phage display;

(7) a kit comprising:

(a) one or more modified nucleotides;

(b) one or more polymerases capable of incorporating the modified nucleotides in a polynucleotide to form a modified polynucleotide; and

(c) a reagent(s) capable of cleaving the modified polynucleotide at each point of occurrence of the modified nucleotides in the polynucleotide.

(8) 24 nucleotide triphosphate derivatives, e.g. nucleotide triphosphate derivatives of formula (I) or (II);

(9) 64 dinucleotide sequences, e.g. dinucleotides of formula (III) or (IV); and

(10) a method of synthesizing dinucleotides.

Base = cytosine, guanine, inosine, thymine or uracil;

X1 = C=O, C(=CH2), or CF2;

X2 = NR, CF2, or CHOH; and

R = not defined.

W = electron withdrawing group.

USE - The methods and kit are useful for the analysis of polynucleotides including detection of variance in nucleotide sequence without the need for full sequence determination, full sequence determination of a polynucleotide, genotyping of DNA and labeling a polynucleotide fragment during the process of cleaving it into fragments.

Dwg.0/40

ABEX UPTX: 20000524

EXAMPLE - A restriction enzyme that has a four base pair recognition site cleaved DNA specifically with a statistical frequency of one cleavage every 256 (44) bases, resulting in fragments that were often too large to be analyzed by mass spectrometry. The chemical dinucleotide restriction strategy resulted in much smaller fragments of the same polynucleotide. The average size of the fragments obtained was 16 (24) bases which was quite amenable to spectrometry analysis.

A dinucleotide pair had a ribonucleotide and 5'-aminonucleotides connected in 5' to 3' orientation, so positioning the 2'-hydroxyl group of the ribonucleotide in close proximity to the phosphoramidate linkage. The chemical lability of the phosphoramidate linker was enhanced since the

hydroxyl group can attack the phosphorous atom to form a 2', 3'-cyclic phosphate, resulting in the cleavage of DNA at this particular dinucleotide site.
A 5'-32P labeled 20 nucleotide (nt) primer was extended with a mixture of Klenow (exo-) and E710A Klenow (exo-) polymerases using a 87nt single stranded template in a Tris buffer at pH9. The primer extension was performed with riboGTP, 5'-aminoTTP, or riboGTP/5'-aminoTTP in place of the corresponding natural nucleotides. After the extension, the reaction mixtures were purified on a G25 column. The riboG-containing extension product was cleaved with aqueous base to generate a G sequencing ladder. The 5'-aminoT-containing product was acid labile and was cleaved to afford a T sequencing ladder. Under the conditions of the extension reaction with riboGTP/5'-aminoTTP, a 64nt product was obtained instead of the expected 87nt. Interestingly, the 64nt fragment was one of the dinucleotide cleavage products expected for GT restriction and the only one which should be visible by autoradiography. Acid cleavage of this product produced a T ladder whereas base cleavage generated a G ladder, indicating the successful incorporation of both riboGTP and 5'-aminoTTP into the polynucleotide. From these results it can be concluded that GT restriction cleavage had occurred during the extension and/or workup procedures, most likely due to the synergized lability of the two modified nucleotides. In order to visualize all three expected restriction fragments, the same extension-cleavage experiment was performed in the presence of alpha-32P-dCTP. Three GT restriction fragments were observed with the expected relative mobility and specific radioactivity.

L68 ANSWER 14 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-159870 [14] WPIX
CROSS REFERENCE: 2000-071658 [06]; 2000-115172 [10]; 2000-146880 [13]
DOC. NO. CPI: C2000-049864
TITLE: Method of determining nucleic acid sequence used in cloning and **sequence analysis** comprises formation of a complementary strand by ligation of short labeled oligonucleotides and identification of the bound labels.
DERWENT CLASS: B04 D16
INVENTOR(S): AKHAVAN-TAFTI, H
PATENT ASSIGNEE(S): (LUMI-N) LUMIGEN INC
COUNTRY COUNT: 24
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6013456	A	20000111	(200014)*		21
WO 2000005412	A1	20000203	(200014)	EN	
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA IL JP					
AU 9952052	A	20000214	(200029)		
EP 1017855	A1	20000712	(200036)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2002521036	W	20020716	(200261)		72
EP 1375676	A2	20040102	(200409)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
AU 772995	B2	20040513	(200462)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

US 6013456	A	Cont of	US 1998-121887	19980724
			US 1999-245984	19990205
WO 2000005412	A1		WO 1999-US14160	19990722
AU 9952052	A		AU 1999-52052	19990722
EP 1017855	A1		EP 1999-937170	19990722
			WO 1999-US14160	19990722
JP 2002521036	W		WO 1999-US14160	19990722
			JP 2000-561358	19990722
EP 1375676	A2	Div ex	EP 1999-937170	19990722
			EP 2003-18758	19990722
AU 772995	B2		AU 1999-52052	19990722

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9952052	A	Based on	WO 2000005412
EP 1017855	A1	Based on	WO 2000005412
JP 2002521036	W	Based on	WO 2000005412
EP 1375676	A2	Div ex	EP 1017855
AU 772995	B2	Previous Publ.	AU 9952052
		Based on	WO 2000005412

PRIORITY APPLN. INFO: **US 1998-121887**
19980724; US 1999-245984
19990205; US 1999-241353
19990202; US 1999-241979
19990202

AB US 6013456 A UPAB: 20040928
NOVELTY - Determining the base sequence of a single stranded nucleic acid comprises sequencing a complementary strand using labeled oligonucleotide 5'-monophosphates.

DETAILED DESCRIPTION - A method of sequencing a portion of a single stranded nucleic acid (I) comprises:

(1) providing a reaction mixture of (I), a complementary capture probe/**primer** (CPP) and labeled **oligonucleotide** 5'-monophosphates (ON) all of the same length each carrying a specific label;

(2) hybridizing (I) with the CPP;

(3) ligating the (I)-CPP hybrid to more than one ON in a contiguous manner in one continuous process, to form a complementary strand where ligation will occur only in the presence of hybridized CPP;

(4) removing non-ligated ON;

(5) detecting the bound labels to identify ligated ON from which the sequence of (I) is deduced.

An INDEPENDENT CLAIM is also included for a similar method (A) using many sets of ON but where one labeled ON present in all other sets is excluded from each set, with each set being reacted separately with (I) and CPP. For each set, attached labels are identified to determine the number and base sequence of ligated ON and to deduce the relative position of the excluded ON in the sequence of the complementary strand. The sequence of (I) is deduced from the relative positions of each excluded ON and from the number and base sequence of ligated ON for all sets combined.

USE - The method is used to sequence single-stranded RNA or DNA for which at least a part of the sequence is known (to allow design of CPP). This can be used for cloning, preparing labeled polynucleotides for diagnostic use, mutation analysis and screening, gene expression monitoring and **sequence analysis.**

ADVANTAGE - Synthesis may be primed uni- or bi-directionally from the

primer, and primer-independent ligation does not occur when short ON are used.
Dwg.0/7

ABEX UPTX: 20000320
WIDER DISCLOSURE - Also described are the use of two primers for simultaneous screening of both strands of a nucleic acid and libraries of short ON.

EXAMPLE - Primer-directed pentamer ligation products were obtained using a 700 base pair DNA sequence downstream of immunoglobulin heavy chain joining region (JH) cloned into a plasmid vector as the template. The JH downstream region was amplified by polymerase chain reaction (PCR) and cloned into a plasmid vector which was digested by EcoRI to obtain a sufficient amount of template DNA. Restriction digest products were separated on an agarose gel and the DNA band of interest extracted using a gel extraction kit. The DNA was resuspended in distilled water at 0.5 microgram/ml.
The primer and pentamers used were:
21 mer primer: 5' GAAACCAGCTTCAAGGCACTG 3'
Pentamer 1: 5' Phosphate AGGUasteriskC 3'
Pentamer 2: 5' Phosphate CUasteriskGGA 3'
Pentamer 3: 5' Phosphate GCCUasteriskC 3'
Pentamer 4: 5' Phosphate CCUasteriskAA 3'
Pentamer 5: 5' Phosphate GCCCC 3'-Biotin
Ligations were carried out with 500 ng template, 100 ng primer and 20 ng each pentamer in each 20 microliter ligation reaction. The number of pentamers was increased in each successive ligation reaction to show the size of the ligation product grew in 5 base increments with each addition of a pentamer.
The template-primer-pentamer mix was heated to 94 degrees Centigrade and kept for 5 minutes to allow denaturation of the double-stranded template. The mix was cooled to 60 degrees Centigrade or 65 degrees Centigrade to anneal the primer to the template for 2 minutes. The reaction tubes were cooled to 16 degrees Centigrade and after 2 minutes, ligation buffer and 1U T4 DNA ligase was added and ligated at 16 degrees Centigrade for 2 hours.
The ligation reaction was stopped by adding loading dye and the reactions then electrophoresed on a denaturing polyacrylamide gel along with biotin-labeled oligonucleotide size markers. The DNA was capillary transferred to a nylon membrane, bound with anti-biotin antibody-HRP (horseradish peroxidase) conjugate and detected by reacting with Lumigen PS-3 (a chemiluminescent HRP substrate) and exposing to an x-ray film. The size of the ligated product varied depending on the number of pentamers ligated to the primer.

L68 ANSWER 15 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-116520 [10] WPIX
DOC. NO. CPI: C2000-035600
TITLE: New nucleotide analogs used as detectors of specific enzyme activity and substrates for nucleic acid polymerases.
DERWENT CLASS: B04 D16
INVENTOR(S): BOYCE-JACINO, M T; GOELET, P; SHI, J
PATENT ASSIGNEE(S): (ORCH-N) ORCHID BIOCOMPUTER INC; (ORCH-N) ORCHID BIOSCIENCES INC
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 9964437 A1 19991216 (200010)* EN 36
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG UZ VN YU ZA ZW
AU 9944380 A 19991230 (200022)
US 6287821 B1 20010911 (200154)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9964437	A1	WO 1999-US13256	19990611
AU 9944380	A	AU 1999-44380	19990611
US 6287821	B1	US 1998-95648	19980611

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9944380	A	Based on	WO 9964437

PRIORITY APPLN. INFO: **US 1998-95648**
19980611

AB WO 9964437 A UPAB: 20000228
NOVELTY - New nucleotide analogs comprise a nucleotide linked to a reporter via a **cleavable** linking group and a spacer.
DETAILED DESCRIPTION - Nucleotide analogs of formula (I) are new:
N-L1-L2-Reporter (I)
N = a nucleotide;
L1 = a **cleavable** linking group, where one end of the **cleavable** linking group is attached to the 3' position of the nucleotide;
L2 = represents a spacer linking group; and
Reporter = a chromophore or a pro-fluorescent fluorophore; where the Reporter exhibits greater fluorescence when uncoupled from the compound.
INDEPENDENT CLAIMS are also included for the following:
(1) determining the identity of a nucleotide at at least one preselected site in a target polynucleotide (PN) by:
(a) incubating a target PN (tPN) in the presence of at least one **primer oligonucleotide** (ON), the **primer** having a sequence complementary to a sequence immediately 3' to the preselected site of the tPN, the incubation permitting the primer ON to hybridize to the target ON and to thereby form a hybridized product;
(b) further incubating the hybridized product in the presence of a mixture comprising a polymerase and at least one pro-fluorescent nucleotide species, the incubation permitting the polymerase-mediated template-dependant addition of the nucleotide species onto the 3'-terminus of the hybridized primer ON;
(c) permitting the polymerase to mediate the template-dependant addition of the pro-fluorescent nucleotide species onto the 3'-terminus of the hybridized primer ON, the addition being additionally dependant on the mixture containing a pro-fluorescent nucleotide species that is complementary to a nucleotide present at the preselected site;
(d) permitting the enzymatic hydrolysis of a reporter from the complementary pro-fluorescent nucleotide species; and

(e) determining the identity of the nucleotide at the preselected site from the identity of the reporter;

(2) determining the nucleic acid sequence of a tPN comprising:

(a) steps (a)-(c) as in (1);

(b) permitting the enzymatic hydrolysis of a reporter from the complementary nucleotide species, to restore a 3' end suitable for the polymerase-mediated template-dependant extension of the primer ON by an additional terminator pro-fluorescent nucleotide species;

(c) determining the identity of the nucleotide at the preselected site from the identity of the hydrolyzed reporter;

(d) performing multiple iterations of steps (b)-(d), thereby in each iteration sequentially extending the primer ON by one terminator pro-fluorescent nucleotide, and determining the identity of a next adjacent nucleotide of the tPN from the identity of the hydrolyzed reporter;

(3) a method comprising:

(a) providing in a reaction a 3'-PF-ddNTP species and an enzyme, such that the 3'-PF-ddNTP is utilized as a substrate in the reaction catalyzed by the enzyme, thereby hydrolyzing the reporter of the 3'-PF-ddNTP species, the 3'-PF-ddNTP species being of formula (II), and

(b) detecting the hydrolyzed reporter;

(4) determining cell viability comprising:

(a) providing to a 3'-PF-ddNTP species to a cell, such that hydrolysis of a reporter from the 3'-PF-ddNTP is dependant upon the viability of the cell; the 3'-PF-ddNTP species being of formula (I) as in (3); and

(b) detecting the hydrolyzed reporter:

N-L1'-L2'-Reporter (II)

L1' = at least one **cleavable** linking group selected from NH-C(O)-, NH-C(S)-, CH2CO, O-C(O)-, or OPO3, where one end of the **cleavable** linking group is attached to the 3' position of the nucleotide, and

L2' = at least one spacer linking group selected from -(NH-CO)n- or (OCH2-CH2)n.

USE - The nucleotide analogs can be used as detectors of specific enzyme activity or as terminator and non-terminator substrates for nucleic acid polymerases. They can be used in nucleic acid **sequence analysis**, hybridization reactions, monitoring of reactions or products from PCR, random priming, nick translation, primer extension, reactions to fill in restriction site overhangs, reverse transcriptase reactions, detection of cellular polymerase activity, and cellular DNA replication.

Dwg.0/4

ABEX UPTX: 20000228

EXAMPLE - 3'-Azido-ddTTP is phosphorylated with 2-chloro-4H-1,3,2-benzodioxa-phosphorin-4-one followed by pyrophosphorylation. The 3'-azido group of the product was then reduced to an amino group by a simple Staudinger reaction, using triphenylphosphine (PPh3) in pyridine to produce 3'-NH2-ddTTP (I-3). Rhodamine 110 was monoacetylated with neat acetic anhydride to give 3-acetamido rhodamine. The 6-amino group of the product was then reacted with carbon disulfide and triethylamine (Et3N) to yield the triethylammonium dithiocarbamate, which is treated with 2-chloro-N-methylpyridinium iodide and Et3N at room temperature to yield the corresponding aryl isothiocyanate (II-3). I-3 and II-3 are then coupled by a reaction of the 3' amino group of I-3 with the isothiocyanate group of II-3. The reaction is carried out in a sodium bicarbonate buffer at pH 9.6. The target compound I is then purified by DEAE Sephadex (RTM) ion exchange chromatography.

L68 ANSWER 16 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-013106 [01] WPIX
DOC. NO. CPI: C2000-002437
TITLE: **Analysis** of polynucleotide **sequences**, used particularly for detecting single-nucleotide polymorphisms in disease diagnosis.
DERWENT CLASS: B04 D16
INVENTOR(S): TAYLOR, S
PATENT ASSIGNEE(S): (PACB) PACKARD BIOSCIENCE CO; (TAYL-I) TAYLOR S
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9953102	A1	19991021	(200001)*	EN	63
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9935670	A	19991101	(200013)		
US 2002168645	A1	20021114	(200277)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9953102	A1		WO 1999-US8407	19990416
AU 9935670	A		AU 1999-35670	19990416
US 2002168645	A1	Provisional	US 1998-82063P	19980416
		Provisional	US 1998-84085	19980504
		Cont of	US 1999-293333	19990416
			US 2001-884425	20010619

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9935670	A	Based on	WO 9953102

PRIORITY APPLN. INFO: **US 1998-84085 19980507; US 1998-82063P 19980416;** US 1999-293333 19990416; US 2001-884425 20010619

AB WO 9953102 A UPAB: 20020621
NOVELTY - New methods for the **analysis** of polynucleotide **sequences** (PMSs) use rolling circle amplification and an array of capture probes

DETAILED DESCRIPTION - A novel method of **analyzing** a polynucleotide **sequence** (PNS) in a sample comprises:

(a) providing a sample PNS to be analyzed;

(b) annealing sample PNS to a single-stranded (ss) circular template to yield an annealed circular template, where the ss circular template comprises at least one copy of a nucleotide sequence (NS) complementary to the sample sequence and at least one nucleotide effective to produce a **cleavage** site;

(c) providing the annealed circular template with a **primer**, at least 2 types of **nucleotide** triphosphates, and a polymerase enzyme to yield a ss oligonucleotide (ON) multimer having a sequence comprising the sequence of the sample PNS and **cleavage** site;

(d) providing an array of capture probes, where each of the capture

probes is positionally distinguishable from other capture probes of the array and where each of the capture probes contains a region of unique sequence; and

(e) hybridizing the amplified sample sequence with the array of capture probes, thereby **analyzing** the sample **sequence**.

INDEPENDENT CLAIMS are also included for:

(1) a method of analyzing a sample PNS comprising:

(a) providing an array of ss circular templates, where each of the ss circular templates is positionally distinguishable from other ss circular templates of the array, and where each positionally distinguishable ss circular template includes a unique region complementary to a region of a sample PNS;

(b) contacting a sample PNS with a ss circular template in the array to yield an annealed circular template, where the ss circular template comprises at least one copy of a NS complementary to a region of the sample sequence;

(c) combining the primed circular template with **primer**, at least 2 types of **nucleotide** triphosphates and a polymerase enzyme to yield an ss ON multimer complementary to the ss circular template, where the ON multimer comprises multiple copies of the sample sequence; and

(d) **analyzing** the sample **sequence**;

(2) a method for identifying NSs binding to a target molecule comprising:

(i) providing a collection of circular NSs, the collection including sequences having a randomized sequence region and a known sequence region, where the known sequence region provides a binding site for an ON primer and a **cleavage** recognition site;

(ii) contacting the target molecule with the NS;

(iii) selecting circular NSs which preferentially bind the target molecule;

(iv) amplifying the NSs; and

(v) analyzing the amplified NSs, thereby identifying circular NSs;

(3) an array comprising circular nucleic acid sequences, the molecules disposed at positionally distinguishable positions in the array and where the nucleic acid sequences comprise sequences with randomized and nonrandomized domains;

(4) a method of analyzing a nucleic acid comprising:

(I) providing a first ON;

(II) providing a second ON which has a first region which is complementary to a first portion of the first ON and a second region which is complementary to a second portion of the first ON;

(III) contacting the first ON with the second ON;

(IV) linking the ends of the first ON to form an Ss circular nucleic acid;

(V) providing a polymerase, a **primer**, and **nucleotides** to the ss circular nucleic acid to form an amplified sequence comprising multimers of sequences complementary to the ss circular nucleic acid; and

(VI) analyzing the resulting amplified **sequence**, therefore **analyzing** a nucleic acid;

(5) a probe for analyzing a nucleic acid comprising a nucleic acid sequence having a first region which is complementary to a first portion of a second nucleic acid sequence and a second region which is complementary to a second portion of the second nucleic acid sequence, where the first portion and second portion of the nucleic acid sequence are positioned so that annealing of the nucleic acid sequence to the second nucleic acid sequence positions the 5' end and the 3' end of the second nucleic acid sequence so as to abut each other.

USE - The methods can be used for analyzing PNSs. They can be used to identify specific nucleotides in a nucleic acid sequence. They can be used to identify single-nucleotide polymorphisms (SNPs) or other mutations in DNA and RNA molecules. The methods can also be used to diagnose or stage a disease state, or predisposition to a disease or condition, and can also be used generally in expression profiling or analysis.
Dwg.1,2,3/3

ABEX UPTX: 20000105

EXAMPLE - A probe (10) has an interrogation region (12) at its 5' end. The interrogation region (12) contains about 5 bases of sequence complementary to a sequence in a target sequence (5). The target sequence (5) contains a specific probe-annealing sequence (7) and interrogation sequence (9). The target sequence (5) can be any polynucleotide, e.g. DNA, RNA, cDNA, synthetic or isolated from an organism, or virus. The interrogation sequence (9) in the target sequence can include a region known to contain, or suspected of containing, a polymorphic region such as a single-nucleotide polymorphism (SNP). The polymorphism in the target nucleic acid sequence is denoted by a 'X'. If complementary sequences are present between the interrogation region (12) and the interrogation sequence (9) target sequence (5), the interrogation region (12) hybridizes to the target and be stabilized by contiguous base stacking. The end of the probe (10) corresponding to the interrogation region (1 2) can be ligated to the other end of the probe (10) if its terminal nucleotide 'Y' forms a complementary base pair with the site of the polymorphism 'X' in the interrogation sequence (9) of the target sequence (5). In contrast, the interrogation region (12) is much less likely to stably hybridize to the sequence (5) if there is a mismatch between the terminal nucleotide 'Y' and the nucleotide at position 'X'. In the latter case, the mismatch between the terminal nucleotide in the interrogation region and the target nucleic acid sequence will preclude ligation of the ends of the probe molecule (10). The probe (10) may also contain a rolling circle amplification (RCA) primer sequence (20), which allows for priming of RCA of the circularized probe (10) upon annealing of a complementary RCA primer. The RCA product formed by the rolling circle amplification is labeled by including one or more labeled dNTPs in the amplification reaction. The RCA products can be perfused over an array of custom Cantor-type probes having 5' overhangs, e.g. as in US5503980. For each allele of each polymorphism there is a corresponding immobilized probe in a gel pad or array cell that is complementary to the 5' end of the corresponding RCA product, i.e. for 1000 biallelic polymorphisms there will be at least 2000 array elements. Target nucleic acids containing specific sequences, e.g. alleles carrying specific polymorphisms, are determined by noting which of the microarray locations specific for a given polymorphism contain RCA products.

L68 ANSWER 17 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-115172 [10] WPIX
CROSS REFERENCE: 2000-071658 [06]; 2000-146880 [13]; 2000-159870 [14]
DOC. NO. CPI: C2000-035183
TITLE: Synthesizing nucleic acids, useful for cloning mutation analysis, screening, and monitoring gene expression.
DERWENT CLASS: B04 D16
INVENTOR(S): AKHAVAN-TAFTI, H
PATENT ASSIGNEE(S): (LUMI-N) LUMIGEN INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

US 5998175 A 19991207 (200010)* 23

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5998175	A	US 1998-121887	19980724

PRIORITY APPLN. INFO: **US 1998-121887**
19980724

AB US 5998175 A UPAB: 20000320
NOVELTY - A method for synthesizing **nucleic** acids comprising hybridization of a **primer** with a single stranded **nucleic** acid template under stable conditions to form a primer template hybrid and ligation of at least 1 oligonucleotide 5' monophosphate (OMP) for extension of the double stranded region, is new.

DETAILED DESCRIPTION - A method for synthesizing nucleic acids comprises:

(a) providing a reaction mixture consisting of a single stranded **nucleic** acid template, a **primer** having at least 15 bases which is complementary to a portion of the template, and a number of OMPs (comprising at most 10 bases);

(b) hybridizing the primer with the template under conditions which permit stable hybridization of the primer but not stable hybridization of the OMPs to form a primer-template hybrid having a single stranded region; and

(c) ligating at least 1 of the OMPs in a contiguous manner onto the primer in one continuous process to extend the double stranded region and synthesize a complementary nucleic acid strand.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for synthesizing an immobilized single stranded nucleic acid having a base sequence complementary to a test single stranded nucleic acid on a solid support comprising hybridization of a probe/ **primer** with the test **nucleic** acid strand and ligating a number of OMPs for extending the double stranded region; and

(2) a method for amplifying a portion of double stranded **nucleic** acid using 2 complementary **primers** having at least 15 base pairs complementary to the first and second strand, comprises separating 2 strands, hybridizing the primers under stable conditions and ligating with the OMPs.

USE - The methods are useful for cloning, preparing labeled polynucleotides for diagnostic use, mutation analysis screening, gene expression monitoring and **sequence analysis**. The methods are also useful for diagnostics including detection of infectious agents, food borne pathogens, detection of gene expression in high throughout screening assays and detection of genetic abnormalities, forensic testing of DNA samples from suspected criminals, identity matching of human remains and paternity testing.

ADVANTAGE - The degree and position of label attachment can be precisely controlled. The ability to test multiple mutations in a gene could enable screening for genetic diseases such as cystic fibrosis for which more than 500 mutations have been identified.

Dwg.0/0

ABEX UPTX: 20000228
WIDER DISCLOSURE - Also disclosed as new are the following:
(1) a method for synthesizing labeled polynucleotides with a specified position and degree of label incorporation;
(2) a method for detecting genes, analyzing gene expression and detecting

genetic mutations;
(3) analyzing the base sequence of nucleic acids;
(4) synthesizing multiply labeled nucleic acid where the extent of labeling is controlled and a high density labeling is provided;
(5) sequencing unknown single stranded nucleic acid;
(6) ligating oligomers onto a template bound primer for the purpose of sequence analysis performed using a single label with quantitative analysis;
(7) detecting target nucleic acid by detecting a labeled extended nucleic acid complementary to the target;
(8) a library of short oligonucleotide 5' monophosphates; and
(9) annealing primer oligonucleotide 5' monophosphates to the single stranded template.

EXAMPLE - A polymerase chain reaction (PCR) amplified product of exon 10 of the cystic fibrosis transmembrane regulator (CFTR) gene was purified and resuspended in distilled water at a concentration of 0.5 micro g/micro l. Commercially obtained pentamers bearing 5'-phosphate and primers were designed to be complementary to either the sense or antisense strand of the template. The first pentamer was annealed immediately adjacent to the 3' end of the primer followed by contiguous pentamer addition. Hybridization of pentamer and primer to the template was followed by ligation using T4 DNA ligase. DNA was capillary transferred to a nylon membrane, bound with anti-biotin antibody-HRP conjugate and detected by reaction with lumigen PS-3 and exposure to an X-ray film.

L68 ANSWER 18 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-110627 [10] WPIX
CROSS REFERENCE: 1996-010936 [01]
DOC. NO. CPI: C1998-036472
TITLE: Catalytic RNA for site-specific **cleavage** of nucleic acid or hydrolysis of amide bonds - and ribozyme amidase intermediates, useful e.g. as peptidase(s), antiviral agents and gene regulators.
DERWENT CLASS: B04 D16
INVENTOR(S): JOYCE, G F
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9802583	A1	19980122	(199810)*	EN	215<--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9736660	A	19980209	(199823)		<--
EP 964930	A1	19991222	(200004)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
US 6063566	A	20000516	(200031)		
JP 2000515013	W	20001114	(200062)		201

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 9802583	A1		WO 1997-US12394	19970716
AU 9736660	A		AU 1997-36660	19970716
EP 964930	A1		EP 1997-933494	19970716
			WO 1997-US12394	19970716
US 6063566	A	CIP of	US 1994-242402	19940513
		CIP of	US 1994-270180	19940701
			US 1996-682423	19960717
JP 2000515013	W		WO 1997-US12394	19970716
			JP 1998-506272	19970716

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9736660	A	Based on	WO 9802583
EP 964930	A1	Based on	WO 9802583
US 6063566	A	CIP of	US 5580967
		CIP of	US 5595873
JP 2000515013	W	Based on	WO 9802583

PRIORITY APPLN. INFO: **US 1996-682423 19960717; US 1994-242402 19940513; US 1994-270180 19940701**

AB WO 9802583 A UPAB: 20001130

Catalytic RNA (I) which catalyses site-specific **cleavage** of nucleic acid under physiological conditions includes a sequence derived from a group I intron.

Also claimed are:

(1) composition of at least 2 (I), each **cleaving** a different substrate;

(2) similar catalytic RNA (II) that catalyses hydrolysis of amide ends in a substrate to produce an amino **cleavage** product (A) and ribozyme amidase intermediate (B);

(3) (B) comprising:

(a) ribonucleotide polymer having a sequence from a group I intron plus a 5'-terminal nucleotide containing a 2'-hydroxy ribose residue, and

(b) substrate containing an amide bond and at least 1 amino acid (aa) residues, including a C-terminal aa covalently linked by an ester bond to the 2'-hydroxy of (a), and

(4) a process of specific **cleavage** of single-stranded DNA under physiological conditions by treating with catalytic RNA having deoxyribo-nucleotide activity.

USE - (II) are useful as peptidases and proteases, e.g. in wound debridement, clot dissolution, in detergents or as meat tenderiser.

(I) **cleave** single- and (partly) double-stranded nucleic acid in vitro or in vivo, and are potentially useful as antiviral agents and gene regulators; also to generate defective but still immunogenic viruses (for vaccines); diagnostically to detect mutations in nucleic acid or to identify nucleic acid binding agents; to modulate/terminate reactions initiated by **DNA primers**; to generate truncated transcripts from **DNA**; to modulate therapeutic/diagnostic processes using antisense sequences; in DNA **fingerprinting** and for vector construction.

ADVANTAGE - (I) and (II) are produced by in vitro evolution processes that provide better catalytic performance; broader active temperature and pH ranges; new enzymatic activities or specificities; altered recognition

sites or co-factor requirement.
Dwg.2B1/11

L68 ANSWER 19 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-530861 [45] WPIX
DOC. NO. CPI: C1998-159198
TITLE: Detection of single-base allelic variants - based on S1 nuclease digestion of mismatched hetero-duplexes and their detection after **amplification**.
DERWENT CLASS: B04 D16
INVENTOR(S): FRAYNE, E G
PATENT ASSIGNEE(S): (FRAY-N) FRAYNE CONSULTANTS
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5811239	A	19980922	(199845)*		10<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5811239	A	US 1996-645600	19960513

PRIORITY APPLN. INFO: **US 1996-645600**
19960513

AB US 5811239 A UPAB: 19981111
A method for detecting and **mapping** single base-pair genetic DNA variants in complex or natural sources of DNA, comprises:
(a) amplifying one or more specific segments of DNA via polymerase chain reaction involving two **oligonucleotide primers** complementary to the ends of the segments of DNA;
(b) denaturing the amplified DNA so that both strands of DNA are completely separated;
(c) renaturing the denatured DNA to form heteroduplexes containing DNA mismatches;
(d) digesting the mismatched DNA heteroduplexes with S1 nuclease so that a non-base-paired region is **cleaved** to produce DNA fragments whose lengths correspond to the site of a single base pair mismatch; and
(e) detecting S1 nuclease digestion products via gel electrophoresis and Southern blotting with a labelled complementary nucleic acid probe.
Also claimed is a method for genome **mapping**, comprising:
(a') amplifying a portion of a genetically **mapped** or tagged marker region via polymerase chain reaction;
(b') amplifying a region corresponding to the marker region from a population of individuals;
(c') denaturing the amplified DNA from steps (a') and (b');
(d') renaturing the denatured DNA to form heteroduplexes;
(e') digesting the heteroduplexes with S1 nuclease;
(f') detecting single base-pair or bi-allelic polymorphisms;
(g') determining the size of DNA segments which give the polymorphisms at a frequency of less than 20%; and
(h') distinguishing between parental and precessive alleles in affected individuals by measuring nuclease digestion products that result from the polymorphisms.
USE - The methods are used for detecting genetic abnormalities or

heritable defects or for differentiating viral or bacterial strains from one another, by detecting single-base pair variants in complex sources of DNA. This is done by amplifying sequences form target DNA, and then hybridising these sequences to form hybrid molecules. These are then digested by S1 nuclease, and detected with standard techniques e.g. hybridisation or Southern blotting.

ADVANTAGE - The method does not require prior sequential knowledge of the target DNA, and is not limited by the size or the complexity (e.g. genomic DNA) of the sample DNA.

Dwg.0/1

L68 ANSWER 20 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1995-382723 [49] WPIX
DOC. NO. NON-CPI: N1995-280374
DOC. NO. CPI: C1995-165362
TITLE: Detecting polymorphic restriction sites by polymerase chain reaction (PCR) **amplification** - involves digestion with restriction enzymes and binding fragments to support carrying specific binding member reactive with PCR primer, for rapid, automated diagnostic testing, **fingerprinting**.
DERWENT CLASS: B04 C07 D13 D16 S03
INVENTOR(S): AUSUBEL, F; DAVID, R W; PREUSS, D
PATENT ASSIGNEE(S): (GEHO) GEN HOSPITAL CORP; (STRD) UNIV LELAND STANFORD JUNIOR
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	
WO 9525538	A1	19950928	(199549)*	EN	115	<--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE						
W: AU CA JP US						
AU 9521872	A	19951009	(199603)			<--
EP 812211	A1	19971217	(199804)	EN		<--
R: BE CH DE DK ES FR GB IE IT LI NL SE						

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9525538	A1	WO 1995-US3419	19950317
AU 9521872	A	AU 1995-21872	19950317
EP 812211	A1	EP 1995-914753	19950317
		WO 1995-US3419	19950317

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9521872	A	Based on	WO 9525538
EP 812211	A1	Based on	WO 9525538

PRIORITY APPLN. INFO: **US 1994-210226 19940318**

AB WO 9525538 A UPAB: 19951211
Detecting the presence or absence of a polymorphic restriction site (PRS) in a nucleic acid (I) comprises: (1) amplifying (I) by PCR using primers (P1, P2) flanking PRS, P1 carrying one member (M1) of a specific binding

pair (SBP) and P2 tagged with a label; (2) digesting amplification prods. with restriction endonuclease (RE) corresp. to PRS; (3) treating the resulting **cleavage** prods. with the second member (M2) of SBP immobilised on a support, and (4) measuring label bound to the support; if this is bound then PRS is absent. About 20 variants of this process are claimed. Also new are: (1) method for identifying PRS comprising: (a) digesting DNA with a first RE; (b) ligating to each end of the fragments a first adaptor (A1); (c) digesting the prods. with a second RE; (d) ligating a second adaptor (A2) to each end of the prods.; (e) amplifying prods. of (d) by PCR using primers complementary to A1 and A2 (the second **primer** carrying M1); (f) incubating second **DNA** sample with first RE; (g) ligation with third adaptor (A3) at each end of the fragments; (h) digesting with second RE; (i) denaturing prods. of (e) and (h); (j) combining denatured prods. for hybridisation; (k) treating hybridised prods. with immobilised M2; (l) recovering captured prods. and (m) amplifying them by PCR using a primer complementary to A3; an amplification prod. then indicates a PRS corresp. to second RE; and (2) kits for these processes.

USE - The methods are used e.g. in clinical diagnosis; genomic **mapping**; cloning of genes defined by mutations, DNA **fingerprinting**; crop/livestock breeding programmes; bacterial typing (e.g. to identify Salmonella in foods) and bacterial screening (e.g. for antibiotic resistance).

ADVANTAGE - The methods do not require gel electrophoresis and can be automated for rapid, inexpensive processing of large number of samples. Some variants include internal controls and oligonucleotide probes that bind to internal regions of PCR prods., so serve to purify the prods., reducing background. DNA from any source can be analysed and in bacterial typing there are fewer false positives compared with known PCR methods. Dwg.1/9

L68 ANSWER 21 OF 54 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1995-227399 [30] WPIX
DOC. NO. CPI: C1995-104537
TITLE: **DNA primers** for **amplification** of an antibody gene - and vectors for the preparation of chimeric antibodies.
DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (EIKE) EIKEN KAGAKU KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 07135978	A	19950530	(199530)*		19<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 07135978	A	JP 1993-289633	19931118

PRIORITY APPLN. INFO: **JP 1993-289633 19931118**

AB JP 07135978 A UPAB: 19950804
A 3'- side **DNA primer** for the amplification of an antibody gene which is complementary to the conserved region in the J region of IgG and is complementary to the conserved region in the base

sequence containing the **cleavage** site of a type II restriction enzyme or in the J region of IgG and is selected from the base sequence containing a base sequence in which the **cleavage** site of a type II restriction enzyme is added. Also claimed are: (1) a 5' side terminal combining adaptor of cDNA in which the base sequence contains at least one type II restriction enzyme site, and (2) recombinant vectors pSRL-neo(-lambda) pSRH(-lambda) and pSRIG-neo, each having a restriction **map** as shown in the specification.

USE - The primer can amplify the IgG variable region with no deviation. The vectors are useful for preparing a library for cloning H- or L-chain variable regions. e.g. for preparing chimeric antibodies. Dwg.0/12

L68 ANSWER 22 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:451553 HCAPLUS
DOCUMENT NUMBER: 141:18700
TITLE: High throughput method for sequencing of genetic polymorphisms or mutations using loci-specific primers that create a restriction endonuclease **cleavage** site
INVENTOR(S): Dhallan, Ravinder S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 82 pp., Cont.-in-part of U.S. Ser. No. 93,618.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004106102	A1	20040603	US 2003-376770		20030228
US 2003186239	A1	20031002	US 2002-93618		20020311
US 2004137470	A1	20040715	US 2003-661165		20030911
PRIORITY APPLN. INFO.:			US 2002-360232P	P	20020301
			US 2002-93618	A2	20020311
			US 2002-378354P	P	20020508
			US 2003-376770	A2	20030228
			WO 2003-US6198	A2	20030228
			WO 2003-US27308	A1	20030829

ED Entered STN: 04 Jun 2004
AB The invention provides a method useful for determining the sequence of large nos. of loci of interest on a single or multiple chromosomes. The method utilizes an oligonucleotide primer that contains a recognition site for a restriction enzyme such that digestion with the restriction enzyme generates a 5' overhang containing the locus of interest. The 5' overhang is used as a template to incorporate nucleotides, which can be detected. The method is especially amenable to the anal. of large nos. of sequences, such as single nucleotide polymorphisms, from one sample of nucleic acid. The examples of the invention provide primers and methods for genotyping human SNPs (single nucleotide polymorphisms) and for detecting mutations in the human APC gene at codons 1302 and 1370 that are associated with colorectal cancer.

L68 ANSWER 23 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:202827 HCAPLUS
DOCUMENT NUMBER: 138:216463
TITLE: polymorphism detection by bi-directional primer extension with labeled terminator nucleotides
INVENTOR(S): Kunkel, Mark; Gelfand, Craig
PATENT ASSIGNEE(S): Orchid Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020950	A2	20030313	WO 2002-US27262	20020827
WO 2003020950	A3	20030417		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003077584	A1	20030424	US 2001-941138	20010828

PRIORITY APPLN. INFO.: US 2001-941138 A 20010828
ED Entered STN: 14 Mar 2003
AB The present invention provides methods and compns. for detecting polymorphic sites by employing bi-directional primer extension reactions. In one embodiment, the present invention provides methods and compns. that minimize cost of reagents, such as labeled nucleotides, and minimize the cost of detection instrumentation. The term bidirectional or bidirectionally refers to primer extension occurring in an antiparallel fashion with respect to the upper and lower primers. Preferably, this bidirectional primer extension is done substantially simultaneously in one reaction well. Accordingly, the method of the present invention is adaptable for multiplex, high throughput genotyping of one or more alleles. The bidirectional SNP detection method of the present invention in one embodiment, employs both upper and lower strand primers, one or more labeled nucleotides, and a single color label that can be detected by a single channel detection device. Primer separation is based upon unique primer tag features that allows for the economical determination of polymorphic site. Advantages of the bidirectional single color reaction scheme of this invention, over the standard multicolor reaction scheme, are illustrated in Table A. Table A shows that the standard multicolor protocol requires the use of labeled nucleotides bearing different detectable signals, whereas the bidirectional single color scheme allows for one kind of detectable signal to be employed on any labeled nucleotides used in the assay. It is advantageous to employ nucleotides with only one kind of detectable characteristic in that it allows detection by a single channel detection device. Such devices are generally more economical than multichannel detection devices. Also, Table A also reveals that for two biallelic polymorphisms, A/T and G/C, only a single labeled nucleotide is required to successfully interrogate those alleles. This effectively reduces the cost of interrogating those alleles in half, because the majority of the cost of carrying out an interrogation reaction is associated with the cost of

the labeled nucleotide.

L68 ANSWER 24 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:667359 HCAPLUS
DOCUMENT NUMBER: 139:208738
TITLE: Methods for high throughput screening of genetic polymorphisms in nucleic acids by primer extension
INVENTOR(S): Dahlhauser, Paul A.
PATENT ASSIGNEE(S): Genetic Assays, Inc., USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 6,150,105.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6610486	B1	20030826	US 2000-717793	20001120 <--
US 6150105	A	20001121	US 1998-137075	19980820
PRIORITY APPLN. INFO.:			US 1998-137075	A2 19980820 <--

ED Entered STN: 27 Aug 2003
AB The present invention provides a method of detecting nucleotide variation within a nucleic acid, comprising single-stranded extension in the presence of modified nucleotide bases, wherein the modified extension products limit exonuclease activity to the 3'-terminal nucleotide base, hybridizing the variable **length** extension products to a reference nucleic acid, and contacting the hybridizing nucleic acids with an enzyme which can remove and replace the 3'-terminal nucleotide of the extension products in the presence of selected labeled nucleotides. Extension products that terminate with a 3'-nucleotide not hybridizing with the corresponding position on the reference nucleic acid are replaced with one or more nucleotides that do hybridize, so that extension products that had a non-hybridizing nucleotide at the 3'-terminus can be distinguished from those extension products that had a hybridizing nucleotide at that position, thereby detecting nucleotide variation in the nucleic acid. Alternatives of this method are also provided which can also detect mutations in a nucleic acid at the penultimate 3'-terminal position on the single-stranded extension products.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 25 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:637874 HCAPLUS
DOCUMENT NUMBER: 137:180745
TITLE: Nucleotide polymorphism detection with chimeric oligonucleotide primers and nuclease cleavage
INVENTOR(S): Sagawa, Hiroaki; Kobayashi, Eiji; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Shuzo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064833	A1	20020822	WO 2002-JP1222	20020214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1367136	A1	20031203	EP 2002-712338	20020214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004137451	A1	20040715	US 2003-468128	20030815
JP 2004298200	A2	20041028	JP 2004-221749	20040729
PRIORITY APPLN. INFO.:			JP 2001-39268 A	20010215
			JP 2001-40721 A	20010216
			JP 2001-101055 A	20010330
			JP 2001-177381 A	20010612
			JP 2001-290384 A	20010925
			JP 2001-338440 A	20011102
			JP 2001-368929 A	20011203
			JP 2002-565143 A3	20020214
			WO 2002-JP1222 W	20020214

ED Entered STN: 23 Aug 2002

AB Chimeric oligonucleotide primers useful in detecting nucleotide polymorphisms, comprising deoxyribonucleotides and ribonucleotides where 3' end is modified to prevent extension by DNA polymerase, are disclosed. In the presence of a mismatch, the chimeric oligonucleotide is not cleaved by a nuclease, whereas in the absence of a mismatch, it is cleaved by a nuclease, creating a new 3'-terminal for extension by DNA polymerase. Either RNase H or restriction enzymes are used. The chimeric oligonucleotide is labeled with a fluorescent substance, and possibly with a quenching substance, so that its cleavage could by detected by fluorescence polarization. Nucleotide analogs such as deoxyriboinosine nucleotides, deoxyribouracil nucleotides, or (α-S) ribonucleotides, having modification at the 3'-OH group of the **ribose**, are preferably used. Use of the oligonucleotides for genotyping anal. and a kit therefor are claimed. Chimeric oligonucleotide having the 3'-OH group of the nucleotide at 3'-end protected with aminohexyl group and their use in detecting the single nucleotide polymorphisms in human c-Ki-ras gene, or human CYP2C19 gene, combined with RNase HII, are described.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 26 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:444423 HCAPLUS
DOCUMENT NUMBER: 137:16488
TITLE: Analysis of sequence tags with hairpin primers to amplify DNA and add an address sequence to the amplification product
INVENTOR(S): Lizardi, Paul M.; Latimer, Darin R.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: U.S., 42 pp., Cont.-in-part of U.S. 6,261,782. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6403319	B1	20020611	US 2000-637384	20000811
US 6261782	B1	20010717	US 2000-544713	20000406
US 2002106649	A1	20020808	US 2001-855793	20010515
US 6677121	B2	20040113		

PRIORITY APPLN. INFO.: US 1999-148870P P 19990813
US 2000-544713 A2 20000406
US 1999-127932P P 19990406

ED Entered STN: 13 Jun 2002

AB Disclosed is a method for the comprehensive anal. of nucleic acid samples and a detector composition for use in the method. The method involves amplifying nucleic acid fragments of interest using a primer that can form a hairpin structure; sequence-based coupling of the amplified fragments to detector probes; and detection of the coupled fragments. The amplified fragments are coupled by hybridization and coupling, preferably by ligation, to detector probes. A hairpin structure formed at the end of the amplified fragments facilitates coupling of the fragments to the probes. The hairpin sequence can be unique to drive the extension product to a specific probe on a microarray. The method allows detection of the fragments where detection provides some sequence information for the fragments. The method allows a complex sample of nucleic acid to be quickly and easily cataloged in a reproducible and sequence-specific manner. The method can also be used to detect amplified fragments having a known sequence.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 27 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:661659 HCAPLUS
DOCUMENT NUMBER: 135:222335
TITLE: Method for reducing artifacts in nucleic acid amplification using template-deficient oligonucleotides as primers
INVENTOR(S): Dean, Frank B.; Faruqi, A. Fawad
PATENT ASSIGNEE(S): Molecular Staging, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064952	A2	20010907	WO 2001-US6491	20010228
WO 2001064952	A3	20021227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1294933	A2	20030326	EP 2001-913174	20010228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

JP 2003525055	T2	20030826	JP 2001-563639		20010228
PRIORITY APPLN. INFO.:			US 2000-514113	A	20000228
			WO 2001-US6491	W	20010228

ED Entered STN: 10 Sep 2001

AB Disclosed are compns. and methods useful for reducing the formation of artifacts during nucleic acid amplification reactions. The method uses special oligonucleotides, referred to herein as template-deficient oligonucleotides, that cannot serve as a template for nucleic acid synthesis over part of their **length**. This prevents the oligonucleotides from serving as effective templates in the formation of artifacts. The disclosed method involves using a template-deficient oligonucleotide as at least one of the oligonucleotides (preferably a primer) in a nucleic acid amplification reaction, where the template-deficient oligonucleotide comprises one or more template-deficient nucleotides, preferably at or near the 5' end of the template-deficient oligonucleotide. The template-deficient nucleotides include modified nucleotides, derivatized nucleotides and ribonucleotides, such as abasic nucleotides and 2'-O-Me ribonucleotides. The disclosed method is useful for reducing artifacts in any nucleic acid amplification reaction involving oligonucleotides. The disclosed method is effective at reducing non-cycle oligonucleotide-based artifacts. Also disclosed are kits useful for reducing artifacts in nucleic acid amplification reactions. The disclosed kits include a template-deficient oligonucleotide, wherein the template-deficient oligonucleotide comprises one or more template-deficient nucleotides, and a nucleic acid polymerase.

L68 ANSWER 28 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2001:636257 HCAPLUS
DOCUMENT NUMBER:	135:206423
TITLE:	Method (mini-sequencing/primer extension) for identification and characterization of polymorphisms in DNA, use of polymorphic site-specific primer, ddNTP and dNTP nucleotides
INVENTOR(S):	Henriksson, Jan Anders Ragnar; Jonsson, Bo Joergen Anders; Norberg, Leif Torbjoern
PATENT ASSIGNEE(S):	Gemini Genomics P.L.C., UK
SOURCE:	PCT Int. Appl., 38 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062966	A2	20010830	WO 2001-GB828	20010226
WO 2001062966	A3	20020404		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002018999	A1	20020214	US 2001-792415	20010223
PRIORITY APPLN. INFO.:			GB 2000-4396 A	20000224
			GB 2000-24328 A	20001004

ED Entered STN: 31 Aug 2001
AB The invention provides a high throughput method (mini-sequencing/primer extension method), and kits for identification and characterization of polymorphisms in genomic DNA of individuals, including identification of single nucleotide polymorphisms (SNPs), and/or of an insertion, a deletion, an inversion, a substitution, or microsatellite repeat in said DNA. The mini-sequencing/primer extension method uses an unique mixture of nucleotides to produce primer extension fragments of different **length** that are indicative of a particular polymorphic variant at a polymorphic site. The method involves combining the biol. sample with a sequencing primer specific for each polymorphic site and a primer extension prepn, to form an assay mixture, and then determining the **size** of primer extension after incubation. The invention relates that the primer extension preparation includes: (1) a chain terminating nucleotides forming a first nucleotide class; (2) a chain elongating nucleotides forming a second nucleotide class such that the second nucleotide class does not include a nitrogenous base present in the first nucleotide class; and (3) a template-dependent nucleic acid polymerase. The mixture is incubated for a time and at a temperature sufficient to extend each primer by addition of at least one nucleotide. To aid in detection, the primer or the first nucleotide class can be labeled, using a radiolabel, fluorescent label, magnetic label or enzymic label. The invention relates that chromatog. or electrophoresis can be use in the determining step. The method disclosed in the invention was used to characterize a polymorphic position in the β2 adrenergic receptor. Using a primer specific for this region and a Cy5-labeled ddGTP, five of six polymorphic variants were detected.

L68 ANSWER 29 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:137418 HCAPLUS
DOCUMENT NUMBER: 134:188948
TITLE: Analysis of sequence tags with hairpin primers
INVENTOR(S): Lizardi, Paul M.; Latimer, Darin R.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012856	A2	20010222	WO 2000-US22246	20000811
WO 2001012856	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6261782	B1	20010717	US 2000-544713	20000406
US 2002106649	A1	20020808	US 2001-855793	20010515
US 6677121	B2	20040113		
PRIORITY APPLN. INFO.:			US 1999-148870P P	19990813
			US 2000-544713 A	20000406

US 1999-127932P P 19990406

ED Entered STN: 25 Feb 2001

AB Disclosed is a method for the comprehensive anal. of nucleic acid samples and a detector composition for use in the method. The method involves amplifying nucleic acid fragments of interest using a primer that can form a hairpin structure; sequence-based coupling of the amplified fragments to detector probes; and detection of the coupled fragments. The amplified fragments are coupled by hybridization and coupling, preferably by ligation, to detector probes. A hairpin structure formed at the end of the amplified fragments facilitates coupling of the fragments to the probes. The method allows detection of the fragments where detection provides some sequence information for the fragments. The method allows a complex sample of nucleic acid to be quickly and easily cataloged in a reproducible and sequence-specific manner. The method can also be used to detect amplified fragments having a known sequence.

L68 ANSWER 30 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:886850 HCAPLUS
DOCUMENT NUMBER: 136:1606
TITLE: Purification of primer extension products using a primer to which is attached a string of arylboronic acid moieties
INVENTOR(S): Dix, Connie Kim; Hughes, Karin A.; Kaiser, Robert J.; Stolowitz, Mark L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001049438	A1	20011206	US 1999-350053	19990708
US 2004072203	A1	20040415	US 2003-418749	20030416

PRIORITY APPLN. INFO.: US 1999-125611P P 19990319
US 1999-350053 A1 19990708

ED Entered STN: 07 Dec 2001

AB The present invention provides methods for the purification of primer extension products. The purified products are free of contaminants, such as polymerase chain reaction and cycle sequencing reaction constituents, and are also free of template DNA. The products are obtained in a form that is optimal for automated DNA sequencing by slab gel or particularly capillary electrophoresis, and for other anal. methods. The methods involve the use of a primer to which is attached a string of arylboronic acid moieties (such as, for example, phenylboronic acid moieties (PBA))., and which is annealed to a template nucleic acid. The annealed template-primer complex is placed in a reaction mixture that contains a polymerase enzyme, dNTPs, ddNTPs, buffer and salts. The polymerase catalyzes the template-directed addition of nucleotides and a dideoxynucleotides to the 3' end of the primer to create primer extension products that terminate in a dideoxynucleotide residue. Typically, the reaction mixture is then heated to denature the primer extension products from the templates, after which the reaction mixture is cooled and the extension reaction is repeated. This cycle can be repeated numerous times as desired. In the second step, the primer extension products are immobilized by attachment to a PBA complexing moiety (such as salicylhydroxamic acid) that is attached to a solid support. The

resulting complex is separated from the reaction mixture, washed, and the primer extension products are dissociated from the solid support by, for example, heating. Finally, the purified primer extension products are analyzed by, for example, slab gel or capillary electrophoresis. In another embodiment, the invention provides methods for isolating a nucleic acid. The methods involve: (a) contacting a sample comprising the nucleic acid with a probe that comprises a string of arylboronic acid moieties and can hybridize to the nucleic acid, to form a nucleic acid hybrid; (b) contacting the nucleic acid hybrid with a solid support having attached thereto a arylboronic acid complexing moiety to form a complex comprising the nucleic acid hybrid and the solid support; (c) separating the complex from the sample.

L68 ANSWER 31 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:598432 HCAPLUS
DOCUMENT NUMBER: 135:177718
TITLE: Nucleic acid assay using ruthenium labeled primer and DNA polymerase for biotin labeled dNTP incorporation
INVENTOR(S): Heroux, Jeffrey A.; Corcoran, Marta V.; Rao, Savitha M.
PATENT ASSIGNEE(S): Igen International, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001014446	A1	20010816	US 1998-23483	19980213 <--
US 6635418	B2	20031021		
PRIORITY APPLN. INFO.:			US 1998-23483	19980213 <--

ED Entered STN: 17 Aug 2001
AB The present invention relates to a method for the determination of the presence and amount of DNA in a sample. The method is based on the use of a nucleic acid template dependent enzyme in combination with a random primer to generate an enzymic product which incorporates a binding species and a detectable species covalently linked. The basic format for the assay of the subject invention is unique because the protocol utilizes an oligonucleotide having a detectable species (eg ruthenylated hexamer) as a primer for incorporating NTP(s) having a binding species (eg biotin-dNTP) as a capture moiety in a DNA template dependent manner. Specifically, random oligonucleotide hexamers covalently labeled with ruthenium at the 5' end are boiled and snapped-cooled in the presence of template DNA. DNA polymerase I (exonuclease Klenow fragment) is used to covalently incorporate biotin-dNTP, the capture moiety, directly to the ruthenylated-labeled hexamer. Free hexamers and biotin-dNTP are eliminated by a column purification step. The labeled DNA product is then captured using **streptavidin** coated magnetic beads and analyzed (eg using an ORIGEN analyzer, IGEN Inc.). Unknown concns. of DNA are extrapolated from a standard curve generated by the Multicalc Wallac program using a 4 or 5 parameter logistic algorithm. Thus the assay of the subject invention not only detects low picogram amts. of DNA but also overcomes the disadvantages of current methodologies. The Tag-DNA assay of the subject invention improves on current methodol. in several aspects. Tag-DNA assay is not as tech. challenging or labor intensive compared to the assays currently used for detection of 10 pg amts. of DNA. Results

from the assays that can accurately detect 10 pg of DNA have lengthy protocols (8 h-5 days) as compared to Tag-DNA assay (4 h). The Tag-DNA assay has a greater dynamic range for detection of DNA (5-10,000 pg) at a 60 min reaction time than any of the current assays. The range of detecting greater amts. of DNA may be tailored to the requirements of the users by altering the enzyme incubation time. The subject assay can detect DNA larger than 100 base pairs regardless of base sequence or species of DNA. This is in contrast to slot-blot, which detects sequences that bind to the probe, or the threshold system which can only accurately detect DNA greater that 872 base pairs. Addnl., the generation of the signal in the Tag-DNA assay does not require radioactivity or incubation with a signal amplifier or enzyme substrate. Another advantage of the subject method is based on the ability to recount samples initially determined to be off the range of the standard curve. A sample will need to be rerun on slot-blot and threshold if a sample is out of the quantitation range of the standard curve. Thus, Tag-DNA improves on the speed and accuracy for determining the amount of DNA in the sample. Addnl., the results are generated faster due to the ease of the protocol and the short incubation time of the enzyme reaction.

L68 ANSWER 32 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:707182 HCAPLUS
DOCUMENT NUMBER: 133:262270
TITLE: Nucleic acids containing unconventional nucleotide and their **cleavage** from solid supports
PATENT ASSIGNEE(S): Goldsborough, Andrew, Fr.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058329	A1	20001005	WO 2000-GB1190	20000328
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368420	AA	20001005	CA 2000-2368420	20000328
BR 2000009395	A	20011226	BR 2000-9395	20000328
EP 1165585	A1	20020102	EP 2000-914272	20000328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500013	T2	20030107	JP 2000-608029	20000328
NZ 514852	A	20030725	NZ 2000-514852	20000328
NO 2001004641	A	20011127	NO 2001-4641	20010925
PRIORITY APPLN. INFO.:			GB 1999-7245 A	19990329
			WO 2000-GB1190 W	20000328

ED Entered STN: 06 Oct 2000
AB The present invention provides a method of detaching a nucleic acid mol. from a solid support to which it is attached, wherein an unconventional

nucleotide is incorporated at a pre-determined site in said nucleic acid mol., said method comprising selectively **cleaving** said nucleic acid mol. at the site of said unconventional nucleotide. The nucleic acid mol. may be a chimeric mol. comprising a nucleic acid (nucleotide sequence) and another mol. component of a different chemical nature. This aspect of the invention also provides a chimeric mol. (or construct) comprising a nucleotide linker sequence comprising a selectively **cleavable** unconventional nucleotide at a pre-determined site, coupled to a functional group, which may be an affinity binding group or a reporter group. The invention finds utility in a number of applications, for example mol. biol. procedures such as nucleic acid synthesis, amplification or sequencing, nucleic acid isolation or in affinity-based separation or assay procedures.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 33 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:688406 HCAPLUS
DOCUMENT NUMBER: 133:248040
TITLE: Methods for single nucleotide polymorphism (snp) detection
INVENTOR(S): Singh, Sharat; Ullman, Edwin F.
PATENT ASSIGNEE(S): Aclara Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056925	A2	20000928	WO 2000-US6135	20000308
WO 2000056925	A3	20020411		

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-125319P P 19990319
ED Entered STN: 29 Sep 2000
AB Methods and compns. are provided for determining large nos. of single nucleotide polymorphisms in target DNA employing particles having (1) primers complementary to sequences in the target DNA where the next succeeding 3'-nucleotide is a potential single nucleotide polymorphism and coding composition members, where the members are unique for each primer, and (2) differentially labeled terminating nucleotides, where the label permits separation of the terminating nucleotides. Desirably the particles are separated into groups having a common prevalent next succeeding nucleotide. The particles and target DNA are combined under nucleotide extending conditions, the particles separated into groups in accordance with the terminating nucleotide and the coding members identified, so that one knows the sequence and the single nucleotide polymorphism. Various protocols are provided for the determination

L68 ANSWER 34 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:161490 HCAPLUS
DOCUMENT NUMBER: 132:204017
TITLE: Method for the preparation of ZeptoStip reaction compartment assemblies containing serial dilutions of

nucleic acid standards, carrier nucleotides and primers for automated PCR
INVENTOR(S): Koehler, Thomas
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012756	A2	20000309	WO 1999-DE2715	19990827 <--
WO 2000012756	A3	20000518		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19840531	A1	20000309	DE 1998-19840531	19980828
DE 19840531	C2	20030515		
CA 2342581	AA	20000309	CA 1999-2342581	19990827 <--
EP 1108066	A2	20010620	EP 1999-953632	19990827 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002523110	T2	20020730	JP 2000-567739	19990827 <--
PRIORITY APPLN. INFO.:			DE 1998-19840531 A	19980828 <--
			WO 1999-DE2715 W	19990827

ED Entered STN: 10 Mar 2000
AB The invention concerns the preparation of reaction compartment assemblies in the form of 8 compartment strips to carry out reproducible PCRs by using compartments in a 12x8 tube holder; placing serial dilns. of standard nucleotides into the compartments along with carrier nucleotides and the primers; freeze drying the content of the compartments; sealing the compartments with a foil to obtain strips of 8 compartments, called ZeptoStrips. Carrier nucleotides are treated with ultrasound prior adding to the solution Primers are labeled or non-labeled; reaction compartments are **glass** or plastic, e.g. optical PCR tubes. ZeptoStrips can be stored 6-12 mo at room temperature and used for PCR with calibration. The ZeptoStrips are included in test kits.

L68 ANSWER 35 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:220099 HCAPLUS
DOCUMENT NUMBER: 130:247841
TITLE: DNA typing by mass spectrometry with PCR-generated polymorphic DNA repeat markers applicable to forensic and paternity testing
INVENTOR(S): Butler, John M.; Li, Jia; Monforte, Joseph; Becker, Christopher A.
PATENT ASSIGNEE(S): Genetrace Systems, Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9914375	A2	19990325	WO 1998-US19578	19980918 <--

WO 9914375 A3 19990729
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9894003	A1	19990405	AU 1998-94003	19980918 <--
US 6090558	A	20000718	US 1998-157177	19980918 <--
US 6764822	B1	20040720	US 2000-541210	20000403 <--
PRIORITY APPLN. INFO.:			US 1997-59415P P	19970919 <--
			US 1998-157177 A3	19980918 <--
			WO 1998-US19578 W	19980918 <--

ED Entered STN: 08 Apr 1999

AB Claimed is the use of mass spectrometry to detect **length** variation in DNA nucleotide sequence repeats (including variants of common alleles), such as microsatellites and short tandem repeats, and to DNA sequences provided as primers for the anal. of DNA tandem nucleotide repeat polymorphisms at specific loci on specific chromosomes. The present invention is related to the fields of genetic mapping and genetic identity detection, including forensic identification and paternity testing. Newly designed primers are provided which are closer to the repeat regions previously employed for anal. by mass spectrometry, which are immobilized on a support for the generation of products smaller than those used in previous methods.

L68 ANSWER 36 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:64971 HCAPLUS
DOCUMENT NUMBER: 130:120452
TITLE: Modified Sanger nucleic acid sequencing of multiple templates using template-specific labeled primers
INVENTOR(S): Schmidt, Gunter; Thompson, Andrew Hugin
PATENT ASSIGNEE(S): Brax Genomics Limited, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902726	A1	19990121	WO 1998-GB2044	19980713 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9882348	A1	19990208	AU 1998-82348	19980713 <--
EP 994968	A1	20000426	EP 1998-932420	19980713 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6312904	B1	20011106	US 2000-462600	20000410 <--
PRIORITY APPLN. INFO.:			GB 1997-14717 A	19970711 <--

GB 1997-19284	A	19970910	<--
GB 1997-26949	A	19971219	<--
WO 1998-GB2044	W	19980713	<--

ED Entered STN: 01 Feb 1999

AB Claimed is a high-throughput method of generating Sanger sequence termination ladders of multiple templates and methods of separating and analyzing those ladders simultaneously. The method for characterizing nucleic acid, which method comprises generating Sanger ladder nucleic acid fragments from a plurality of nucleic acid templates present in the same reaction zone, at least one terminating base being present in the reaction zone, and for each nucleic acid fragment produced identifying the **length** of the fragment, the identity of the template from which the fragment is derived and the terminating base of the fragment, wherein prior to generating the fragments, a labeled primer nucleotide or oligonucleotide is hybridized to each template, the label on each primer being specific to the template to which that primer hybridizes to allow identification of the template.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 37 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:808578 HCAPLUS
DOCUMENT NUMBER: 132:31745
TITLE: Method for determining nucleotide identity through extension of immobilized primer
INVENTOR(S): Goelet, Philip; Knapp, Michael R.; Anderson, Stephen
PATENT ASSIGNEE(S): Molecular Tool, Inc., USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 5,888,819.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 6004744	A	19991221	US 1991-775786	19911011	<--
US 5888819	A	19990330	US 1991-664837	19910305	
CA 2105060	AA	19920906	CA 1992-2105060	19920304	<--
WO 9215712	A1	19920917	WO 1992-US1905	19920304	<--
W: AU, CA, FI, JP, NO					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
AU 9215848	A1	19921006	AU 1992-15848	19920304	<--
AU 660173	B2	19950615			
EP 576558	A1	19940105	EP 1992-908554	19920304	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
JP 06505394	T2	19940623	JP 1992-508312	19920304	<--
NO 9303136	A	19930902	NO 1993-3136	19930902	<--
US 5762876	A	19980609	US 1994-362266	19941222	<--
US 2003044778	A1	20030306	US 1999-258132	19990226	<--
US 2003044779	A1	20030306	US 1999-258133	19990226	<--
US 6537748	B2	20030325			
FI 2001000223	A	20010207	FI 2001-223	20010207	<--

PRIORITY APPLN. INFO.:	US 1991-664837	A2	19910305 <--
	US 1991-775786	A	19911011 <--
	WO 1992-US1905	A	19920304 <--
	US 1993-145145	B2	19931103 <--
	US 1993-155746	A2	19931123 <--
	US 1993-162397	B2	19931206 <--

US 1993-173173 B2 19931223 <--

ED Entered STN: 23 Dec 1999

AB The invention concerns a reagent composition that employs at least two different terminators of a nucleic acid template-dependent primer extension reaction to determine the identity of a nucleotide base at a specific position in a nucleic acid of interest. These primers are labeled with biotin and hybridization to **streptavidin** is detected. The primers are separated from nucleic acid of interest after the extension step by using denaturing conditions which comprise heat, alkali, formamide, urea, glyoxal, or enzymes or 0.2 N NaOH. The invention also concerns an immobilized method for determining such identification. The invention may be used to determine the presence or absence of a specific nucleotide sequence in a sample. Four terminators are labeled each with a different marker and may comprise a nucleotide or nucleotide analog or dideoxynucleotides or arabinoside triphosphates. A non-natural nucleotide analog may comprise deoxyinosine or 7-deaza-2'-deoxyguanosine. It may also be employed in determination of genotype and in the identification of different alleles. The organism may be a plant or microorganism or virus or bird or vertebrate or invertebrate or mammal or horse or dog or cow or pig or sheep.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 38 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:9955 HCAPLUS
DOCUMENT NUMBER: 130:77062
TITLE: Screening methods for the identification of genetic mutations or disease-causing microorganisms using segmented primers
INVENTOR(S): Shuber, Anthony P.
PATENT ASSIGNEE(S): Exact Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858084	A1	19981223	WO 1998-US12589	19980616 <--
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5888778	A	19990330	US 1997-877333	19970616
AU 9879732	A1	19990104	AU 1998-79732	19980616 <--
AU 744746	B2	20020228		
EP 1000173	A1	20000517	EP 1998-930316	19980616 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002510206	T2	20020402	JP 1999-504733	19980616 <--

PRIORITY APPLN. INFO.: US 1997-877333 A 19970616 <--
WO 1998-US12589 W 19980616 <--

ED Entered STN: 07 Jan 1999

AB Methods are provided for high-throughput screening for the presence of genetic alterations (insertions, deletions, mutations, or the presence of a gene/gene locus known to be involved in a pathol. condition or syndrome) and disease-causing microorganisms in a biol. sample. The provided methods are based upon the use of segmented primers, which comprise at least two oligonucleotide probes of differing size and m.p. that are

capable of hybridizing to substantially contiguous portions of a targeted nucleic acid. The first probe hybridizes with high selectivity but forms unstable hybrids when alone, and the second probe forms a stable hybrid but has a lower selectivity. The segmented probes are used by polymerase to generate a primer that hybridizes with the high selectivity of the first probe and has the high stability of the second probe, and this primer is used for the aforementioned screening applications. Also provided are methods for the early detection of colon cancer by detection of alterations in the c-Ki-ras gene.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 39 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:731816 HCAPLUS
DOCUMENT NUMBER: 129:340523
TITLE: Method for evaluation allelic subtype of known polymorphic genetic locus using oligonucleotide primers and chain-terminating nucleotides, especially as applied for HLA antigen typing
INVENTOR(S): Stevens, John K.; Dunn, James M.; Leushner, James; Green, Ronald J.
PATENT ASSIGNEE(S): Visible Genetics Inc., Can.
SOURCE: U.S., 118 pp., Cont.-in-part of U.S. 5,545,527.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5834189	A	19981110	US 1995-577858	19951222 <--
US 5545527	A	19960813	US 1994-271946	19940708 <--
US 5853979	A	19981229	US 1995-497202	19950630 <--
CA 2239896	AA	19970703	CA 1996-2239896	19961219 <--
WO 9723650	A2	19970703	WO 1996-US20202	19961219 <--
WO 9723650	A3	19970821		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9714262	A1	19970717	AU 1997-14262	19961219 <--
AU 718670	B2	20000420		
EP 870059	A2	19981014	EP 1996-944459	19961219 <--
EP 870059	B1	20020417		
R: CH, DE, FR, GB, LI, SE				
JP 2000502260	T2	20000229	JP 1997-523796	19961219 <--
CA 2240831	AA	19970717	CA 1997-2240831	19970106 <--
WO 9724974	A2	19970717	WO 1997-CA6	19970106 <--
WO 9724974	A3	19971127		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF
AU 9711875 A1 19970801 AU 1997-11875 19970106 <--
EP 871779 A2 19981021 EP 1997-900057 19970106 <--
R: CH, DE, FR, GB, LI, SE
US 5888736 A 19990330 US 1997-807138 19970227 <--
WO 9741257 A1 19971106 WO 1997-US7133 19970429 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
US 5981186 A 19991109 US 1997-892003 19970714 <--
US 6007983 A 19991228 US 1997-938641 19970926 <--
US 6265152 B1 20010724 US 1999-418720 19991015 <--
US 2003165815 A1 20030904 US 2001-818182 20010327 <--
US 6653107 B2 20031125
US 2003022190 A1 20030130 US 2001-32924 20011226 <--
PRIORITY APPLN. INFO.: US 1994-271946 A2 19940708 <--
US 1995-497202 A2 19950630 <--
US 1995-577858 A 19951222 <--
US 1996-583289 A 19960105 <--
US 1996-640672 A2 19960501 <--
US 1996-649950 A1 19960514 <--
US 1996-670534 A2 19960627 <--
US 1996-684498 A2 19960719 <--
US 1996-699628 A 19960819 <--
WO 1996-US20202 W 19961219 <--
WO 1997-CA6 W 19970106 <--
US 1997-807138 A2 19970227 <--
US 1997-819912 A2 19970318 <--
US 1997-938641 A2 19970926 <--
US 1999-418720 A1 19991015

ED Entered STN: 18 Nov 1998

AB The allelic type of a polymorphic genetic locus in a sample is identified by first combining the sample with a sequencing reaction mixture containing a polymerase, nucleotide feedstocks, one type of chain-terminating nucleotide and a sequencing primer to form a plurality of oligonucleotide fragments of differing **lengths**, and then evaluating the **length** of the oligonucleotide fragments. As in a standard sequencing procedure, the **lengths** of the fragments indicate the positions of the type of base corresponding to the chain-terminating nucleotide in the extended primer. Instead of performing and evaluating 4 concurrent reactions, one for each type of chain-terminating nucleotide, however, the sample is concurrently combined with at most 3, and preferably only one, sequencing reaction mixts. containing different types of chain-terminating nucleotides. The information obtained from this test is evaluated prior to performing any addnl. tests on the sample. In many cases, evaluation of the positions of only a single base using one sequencing reaction will allow for allelic typing of the sample.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 40 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:411418 HCAPLUS
DOCUMENT NUMBER: 127:104875

TITLE: Minisequencing: a specific tool for DNA analysis and diagnostics on oligonucleotide arrays
AUTHOR(S): Pastinen, Tomi; Kurg, Ants; Metspalu, Andres; Peltonen, Leena; Syvanen, Ann-Christine
CORPORATE SOURCE: Dep. Human Mol. Genetics, Natl. Public Health Inst., Helsinki, 00300, Finland
SOURCE: Genome Research (**1997**), 7(6), 606-614
CODEN: GEREFS; ISSN: 1088-9051
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 Jul 1997
AB We describe a method for multiplex detection of mutations in which the solid-phase minisequencing principle is applied to an oligonucleotide array format. The mutations are detected by extending immobilized primers that anneal to their template sequences immediately adjacent to the mutant nucleotide positions with single labeled dideoxynucleoside triphosphates using a DNA polymerase. The arrays were prepared by coupling one primer per mutation to be detected on a small **glass** area. Genomic fragments spanning nine disease mutations, which were selected as targets for the assay, were amplified in multiplex PCR reactions and used as templates for the minisequencing reactions on the primer array. The genotypes of homozygous and heterozygous genomic DNA samples were unequivocally defined at each analyzed nucleotide position by the highly specific primer extension reaction. In a comparison to hybridization with immobilized allele-specific probes in the same assay format, the power of discrimination between homozygous and heterozygous genotypes was one order of magnitude higher using the minisequencing method. Therefore, single-nucleotide primer extension is a promising principle for future high-throughput mutation detection and genotyping using high d. DNA-chip technol.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L68 ANSWER 41 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:369799 HCAPLUS
DOCUMENT NUMBER: 125:27663
TITLE: Allelic variation of the serotonin 5HT2C receptor containing serine-23 and PCR correlation of variant with neuropsychiatric disorders
INVENTOR(S): Lappalainen, Jaakko; Linnoila, Markku; Goldman, David
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9609386	A2	19960328	WO 1995-US12002	19950921 <--
WO 9609386	A3	19960502		

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,

SN, TD, TG

US 5654139	A	19970805	US 1994-310271	19940921 <--
CA 2199470	AA	19960328	CA 1995-2199470	19950921 <--
AU 9537203	A1	19960409	AU 1995-37203	19950921 <--
AU 693944	B2	19980709		
EP 782618	A2	19970709	EP 1995-935029	19950921 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 11507802	T2	19990713	JP 1995-511070	19950921 <--
PRIORITY APPLN. INFO.:			US 1994-310271 A	19940921 <--
			WO 1995-US12002 W	19950921 <--

ED Entered STN: 27 Jun 1996
AB Isolated DNA encoding the serotonin 5HT2C receptor with serine at amino acid position 23, antibody specific to such a variant receptor and the variant receptor protein itself are used in methods for detecting the presence of an allelic variant of the serotonin 5HT2C gene or receptor.

L68 ANSWER 42 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:363513 HCAPLUS
DOCUMENT NUMBER: 125:27659
TITLE: Pathogenic mycobacteria specific, sensitive, and rapid detection by genomic DNA amplification and hybridization with oligonucleotide probe and use for infection diagnosis
INVENTOR(S): Murray, Alan; Gormley, Eamonn Patrick
PATENT ASSIGNEE(S): N. Z.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9608579	A1	19960321	WO 1995-NZ89	19950918 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9536210	A1	19960329	AU 1995-36210	19950918 <--
PRIORITY APPLN. INFO.:			NZ 1994-264473	19940916 <--
			WO 1995-NZ89	19950918 <--

ED Entered STN: 22 Jun 1996
AB This invention relates to methods of detecting pathogenic mycobacteria with reference to a characteristic 152 bp DNA sequence. Identification of the specific species of pathogenic mycobacteria is also possible through reference to both the characteristic DNA sequence above and the genomic DNA which flanks it in that particular species.

L68 ANSWER 43 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:161560 HCAPLUS
DOCUMENT NUMBER: 124:281084
TITLE: Diagnosis and treatment of conditions related to telomere **length** or telomerase activity
INVENTOR(S): West, Michael D.; Shay, Jerry; Wright, Woodring
PATENT ASSIGNEE(S): Board of Regents of the University of Texas System,

	USA
SOURCE:	U.S., 39 pp. Cont.-in-part of U.S. Ser. No. 882,438, abandoned.
	CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	21

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5489508	A	19960206	US 1993-38766	19930324 <--
WO 9323572	A1	19931125	WO 1993-US4546	19930513 <--
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9343740	A1	19931213	AU 1993-43740	19930513 <--
AU 688262	B2	19980312		
EP 642591	A1	19950315	EP 1993-913867	19930513 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08501079	T2	19960206	JP 1994-503742	19930513 <--
US 5695932	A	19971209	US 1993-60952	19930513 <--
JP 11123100	A2	19990511	JP 1998-226268	19930513 <--
JP 11127874	A2	19990518	JP 1998-226303	19930513 <--
JP 2000116388	A2	20000425	JP 1999-286016	19930513 <--
CA 2245461	C	20010626	CA 1993-2245461	19930513 <--
JP 2002101898	A2	20020409	JP 2001-222342	19930513 <--
CA 2135648	C	20020625	CA 1993-2135648	19930513 <--
CA 2245462	C	20020625	CA 1993-2245462	19930513 <--
US 5645986	A	19970708	US 1993-153051	19931112 <--
US 5830644	A	19981103	US 1993-151477	19931112 <--
US 5989807	A	19991123	US 1994-255774	19940607 <--
US 5648215	A	19970715	US 1994-315216	19940928 <--
US 5744300	A	19980428	US 1994-332420	19941031 <--
US 5686306	A	19971111	US 1994-337684	19941110 <--
US 6368789	B1	20020409	US 1995-464011	19950605 <--
US 2002127634	A1	20020912	US 1995-463404	19950605 <--
US 5686245	A	19971111	US 1995-475778	19950607 <--
US 5693474	A	19971202	US 1995-486042	19950607 <--
US 5707795	A	19980113	US 1995-487290	19950607 <--
US 5837453	A	19981117	US 1995-482132	19950607 <--
US 5840495	A	19981124	US 1995-480037	19950607 <--
US 6194206	B1	20010227	US 1997-998876	19971224 <--
AU 9871836	A1	19980820	AU 1998-71836	19980612 <--
AU 726528	B2	20001109		
AU 9889495	A1	19990107	AU 1998-89495	19981023 <--
AU 9889496	A1	19990114	AU 1998-89496	19981023 <--
AU 735840	B2	20010719		
US 6551774	B1	20030422	US 1999-378535	19990820 <--
US 6391554	B1	20020521	US 1999-447151	19991123 <--
US 2003190638	A1	20031009	US 2002-232927	20020829 <--
US 2003175766	A1	20030918	US 2002-323032	20021218 <--
US 2004198659	A1	20041007	US 2003-691633	20031022 <--

PRIORITY APPLN. INFO.:	US 1992-882438	B2	19920513 <--
	US 1993-38766	A	19930324 <--
	CA 1993-2135648	A3	19930513 <--
	JP 1993-503742	A3	19930513 <--
	JP 1998-226303	A3	19930513 <--
	US 1993-60952	A2	19930513 <--

WO 1993-US4546	A	19930513 <--
US 1993-151477	A2	19931111 <--
US 1993-153051	A2	19931111 <--
US 1994-235180	A2	19940429 <--
US 1994-255774	A2	19940607 <--
US 1994-315214	A2	19940928 <--
US 1994-315216	A2	19940928 <--
US 1995-423403	A2	19950418 <--
US 1995-463404	B1	19950605 <--
US 1995-483144	A1	19950607 <--
US 1997-819867	A1	19970314 <--
AU 1998-71836	A3	19980612 <--
US 1999-378535	A3	19990820

ED Entered STN: 20 Mar 1996

AB A method and reagents for the determination of telomere **length** and telomerase activity are described for use in the treatment of proliferative disease. Methods of inhibiting telomerase activity in the treatment of proliferative diseases are also described. Primers that are elongated under conditions that minimize interference from other genomic sequences are used to obtain accurate detns. of telomere **length** or telomerase activity. In addition, compns. are provided for intracellular inhibition of telomerase activity. A relationship between telomere **length** and cell senescence was demonstrated in tissue culture cells. The inhibition of telomerase by an oligonucleotide complementary to the endogenous telomerase template is demonstrated.

L68 ANSWER 44 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:572067 HCAPLUS
DOCUMENT NUMBER: 125:214233
TITLE: Use of exonuclease and/or glycosylase as supplements to thermally labile anti-polymerase antibody to increase specificity in polymerase chain reaction
INVENTOR(S): Sutherland, John W. H.; Patterson, David R.
PATENT ASSIGNEE(S): Johnson and Johnson Clinical Diagnostics, Inc., USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 726324	A2	19960814	EP 1996-300791	19960206 <--
EP 726324	A3	19961127		
EP 726324	B1	20010523		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2168712	AA	19960808	CA 1996-2168712	19960202 <--
FI 9600540	A	19960808	FI 1996-540	19960206 <--
NO 9600484	A	19960808	NO 1996-484	19960206 <--
AU 9643391	A1	19960815	AU 1996-43391	19960206 <--
AU 709788	B2	19990909		
JP 08266298	A2	19961015	JP 1996-20082	19960206 <--
ES 2156978	T3	20010801	ES 1996-300791	19960206 <--
PT 726324	T	20010830	PT 1996-300791	19960206 <--
US 5985619	A	19991116	US 1996-643282	19960508 <--
GR 3036391	T3	20011130	GR 2001-401247	20010814 <--
PRIORITY APPLN. INFO.:			US 1995-385019 A	19950207 <--

ED Entered STN: 26 Sep 1996

AB The present invention provides admixts. and methods for PCR amplification of a target nucleic acid in which amplification efficiency is increased by including an antibody specific for a polymerization agent and at least one of an exonuclease and a glycosylase in the PCR reaction mix. Kits for amplification of a target nucleic acid are also provided.

L68 ANSWER 45 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:473259 HCAPLUS
DOCUMENT NUMBER: 125:137357
TITLE: Structural Variation among Retroviral Primer-DNA Junctions: Solution Structure of the HIV-1 (-)-Strand Okazaki Fragment r(gcca)d(CTGC)·d(GCAGTGGC)
AUTHOR(S): Fedoroff, Oleg Yu.; Salazar, Miguel; Reid, Brian R.
CORPORATE SOURCE: Chemistry Department, University of Washington, Seattle, WA, 98195, USA
SOURCE: Biochemistry (**1996**), 35(34), 11070-11080
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 10 Aug 1996
AB The three-dimensional solution structure of the hybrid-chimeric duplex r(gcca)d(CTGC)· d(GCAGTGGC) has been determined by two-dimensional NMR, restrained mol. dynamics (rMD), and NOE back-calcn. methods. This chimera, consisting of a chimeric RNA-DNA strand and its complementary DNA strand, is formed after priming (-)-strand DNA synthesis by tRNALys3 and subsequent (+)-strand DNA synthesis by reverse transcriptase and is an obligatory intermediate in the formation of double-stranded DNA prior to HIV-1 retrovirus integration. The duplex consists of two different types of double helix: a hybrid form (H-form) and a B-form structure connected by a junction. It is chemical similar to several other Okazaki fragments whose structures have been previously determined in our laboratory However, some structural parameters are not the same and were found to be sequence dependent. In particular, the **sugar** conformations at the DNA base pair proximal to the hybrid segment vary from O4'-endo to C2'-endo depending on the base composition The position of the transition from the relatively wide groove of H-form to the narrow groove of B-form is also sequence dependent, occurring either exactly at the RNA-DNA junction or within the purely DNA segment of the chimera-as is the case in the structure of the present HIV-1 (-)-strand primer. This structural change produces a kink at the DNA-DNA step adjacent to the RNA-DNA junction in the HIV-1 (-)-strand primer. The sequence dependence of structures of RNA-DNA chimeric duplexes may be responsible for the variable cleavage pattern of different Okazaki fragments by reverse transcriptase RNase H.

L68 ANSWER 46 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:578878 HCAPLUS
DOCUMENT NUMBER: 125:213559
TITLE: An efficient PCR mutagenesis strategy without gel purification step that is amenable to automation
AUTHOR(S): Seraphin, Bertrand; Kaneels-Lewis, Stefanie
CORPORATE SOURCE: EMBL, Heidelberg, D-69117, Germany
SOURCE: Nucleic Acids Research (**1996**), 24(16), 3276-3277
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 28 Sep 1996
AB We describe here an improved megaprimer PCR mutagenesis strategy. The cumbersome gel purification step that is usually used can be omitted by appropriately **cleaving** the first and second DNA templates with restriction enzymes and enzymically removing remaining primers from the first PCR reaction. We show that this improved procedure is reproducible and highly efficient. Furthermore this method is suitable for automation because all the steps are now carried out in reaction tubes.

L68 ANSWER 47 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:102609 HCAPLUS
DOCUMENT NUMBER: 124:137803
TITLE: Genome nucleic acid amplification and electric signal analysis for genotyping and use in genetic mapping or disease diagnosis
INVENTOR(S): Perlin, Mark W.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9535542	A1	19951228	WO 1995-US8540		19950614	<--
W: CA, JP, US						
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
US 5580728	A	19961203	US 1994-261169		19940617	<--
EP 714537	A1	19960605	EP 1995-926200		19950614	<--
R: DE, FR, GB, IT, NL						
US 6054268	A	20000425	US 1996-734717		19961021	<--
PRIORITY APPLN. INFO.:			US 1994-261169	A	19940617	<--
			WO 1995-US8540	W	19950614	<--

ED Entered STN: 20 Feb 1996
AB Method for genotyping comprising obtaining nucleic acid material, amplifying a location of a material and assaying the amplified material by converting the material into a first set of elec. signals corresponding to **size** and concentration of the amplified products. The first set of elec. signals are operated on with a second set of elec. signals to produce a third set of clean elec. signals corresponding to the **size** and multiplicities of the unamplified material at the location. A system for genotyping is disclosed comprising a mechanism for using said method. The assaying mechanism is in communication with the amplifying mechanism. A converting mechanism in communication with the assaying mechanism converts the material into a first set of elec. signals corresponding to the **size** and concentration of the amplified product. An operating mechanism is provided which operates on a first set of elec. signals with a second set of signals corresponding to a response pattern of the location to produce a third set of clean elec. signals corresponding to the **size** and multiplicities of the unamplified material at the location. A method for analyzing genetic material and producing a gene is also disclosed.

L68 ANSWER 48 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:758775 HCAPLUS
DOCUMENT NUMBER: 123:135083

TITLE: Use of strand displacement amplification to detect nucleic acids in cells
INVENTOR(S): Singer, Robert H.; Lohman, Kenton L.; Mathys, Jean-Marie
PATENT ASSIGNEE(S): Becton Dickinson and Co., USA; University of Massachusetts medical Center
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 657548	A1	19950614	EP 1994-309308	19941212 <--
EP 657548	B1	20010307		
R: DE, FR, GB, IT, NL				
US 5523204	A	19960604	US 1993-165719	19931210 <--
AU 9480221	A1	19950615	AU 1994-80221	19941206 <--
AU 696381	B2	19980910		
CA 2137760	AA	19950611	CA 1994-2137760	19941209 <--
JP 08033500	A2	19960206	JP 1994-307877	19941212 <--
PRIORITY APPLN. INFO.:			US 1993-165719 A	19931210 <--

ED Entered STN: 26 Aug 1995
AB Methods for using the strand displacement amplification (SDA) reaction for amplification of nucleic acid target sequences in situ in cells in suspension, on slides or in tissues are described. Excellent specimen morphol. is preserved when fixed, permeabilized cells are used, and either DNA targets, or RNA targets, or both may be selectively amplified. In situ amplification by SDA is comparable with immunochem. techniques, so that both amplification of target sequences and immunol. staining can be performed on the same specimen. A denaturation step can be used to detect double-stranded nucleic acids or the denaturation step can be omitted to detect single-stranded nucleic acids. Products are detected by nucleic acid hybridization with a labeled probe. A probe conjugated with an enzyme allows efficient detection and quantitation of the target sequence.

L68 ANSWER 49 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:699331 HCAPLUS
DOCUMENT NUMBER: 125:319594
TITLE: Characterization of minisatellite sequences in rice and their application for DNA fingerprinting
AUTHOR(S): Zhou, Z.; Gustafson, J. P.
CORPORATE SOURCE: Department Agronomy, University Missouri, Columbus, MO, USA
SOURCE: Induced Mutations and Molecular Techniques for Crop Improvement, Proceedings of an International Symposium on the Use of Induced Mutations and Molecular Techniques for Crop Improvement, Vienna, June 19-23, 1995 (**1995**), 205-214. International Atomic Energy Agency: Vienna, Austria.
CODEN: 63NLAP
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 25 Nov 1996
AB Mol. markers offer significant value in helping breeding programs to characterize and evaluate genetic variability in germplasm and to identify variety. However, use of restriction fragment **length**

polymorphism (RFLP) and random amplified polymorphic DNA (RAPD) markers can require up to and more than 40 markers and several enzyme combinations in order to identify variation in germplasm. Therefore, rice minisatellite probes were evaluated for their potential in detecting DNA fingerprints and in assessing genetic variation in the genus Oryza. Fifty-seven cultivars of rice from around the world, including 40 closely related cultivars released in the United States of America, were evaluated. DNA fingerprinting detected high levels of polymorphism among cultivars. The variability in fingerprinting patterns was greatly reduced in closely related cultivars. The polymerase chain reaction (PCR), with minisatellite core sequences as primers, was also employed to detect genetic variation in the genus Oryza. It was demonstrated that DNA fingerprinting with minisatellite sequences is simpler and more sensitive than most other types of marker system in detecting genetic variation in cultivated rice. PCR application with directed amplification of mini-satellite region DNA represents a potential tool for identifying species in the genus Oryza.

L68 ANSWER 50 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:200438 HCAPLUS
DOCUMENT NUMBER: 122:2783
TITLE: Methods for producing metal-binding antibodies and pharmaceutical compositions containing the antibodies
INVENTOR(S): Barbas, Carlos F.; Rosenblum, Jonathan; Lerner, Richard A.
PATENT ASSIGNEE(S): Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9418220	A1	19940818	WO 1994-US1238		19940202	<--
W: AU, CA, FI, JP, NO						
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
US 5679548	A	19971021	US 1993-77797		19930614	<--
AU 9461703	A1	19940829	AU 1994-61703		19940202	<--
PRIORITY APPLN. INFO.:			US 1993-12566	A	19930202	<--
			US 1993-77797	A	19930614	<--
			WO 1994-US1238	W	19940202	<--

ED Entered STN: 19 Nov 1994
AB The present invention describes methods for producing metal binding sites on polypeptides, and particularly for producing metal binding sites within the CDR regions of Ig heavy or light chains that are displayed on the surface of filamentous phage particles. The method comprises mutagenesis of the CDR of Ig heavy or light chain genes by amplifying the CDR region by a primer extension reaction using primer oligonucleotides consisting of a 3' terminus and a 5' terminus capable of hybridizing with the framework region of the Ig gene and a sequence between the termini consisting of (NNS)a (N=any nucleotide; S=G,C; a=3-50). Chimeric Ig genes are prepared using the amplified CDR's and these genes are expressed in an appropriate host cell. The recombinant Ig's are selected for their ability to bind to preselected metal ion-containing mols. The invention also describes oligonucleotides useful for preparing the metal binding sites, and human monoclonal antibodies produced by the present methods. Recombinant Fab's with formation consts. of 10-7M for Ni-bovine serum albumin complexes were

prepared

L68 ANSWER 51 OF 54 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:398153 HCAPLUS
DOCUMENT NUMBER: 125:106092
TITLE: HLA-DRB typing using PCR-MPH (microtiter plate-hybridization)
AUTHOR(S): Kawai, Shintaro; Maekawajiri, Shinji; Tokunaga, Katsushi; Miyamoto, Masaki; Akaza, Tatsuya; Juji, Takeo; Yamane, Akio
CORPORATE SOURCE: Institute Biotechnology Research, Wakunaga Pharmaceutical Co., Ltd., Hiroshima, Japan
SOURCE: MHC, Major Histocompatibility Complex (**1994**), 1(Suppl.), 121-125
CODEN: MMHCFQ
PUBLISHER: Nippon Soshiki Tekigosei Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 11 Jul 1996
AB HLA class II allele identification using PCR-microtiter plate-hybridization (PCR-MPH) methods are described. PCR is performed for the second exon of the DRB gene with biotinylated primers. Amplified DNA is hybridized to immobilized probes under discriminatory conditions for nucleotide substitutions. Finally, the biotinylated DNA bound to the immobilized probes on the microtiter well is detected colorimetrically by means of the standard biotin-**streptavidin** method. Improved generic probes were used to achieve allelic typing by this method. The method is demonstrated by allelic typing of DR4 and Dr6. Typing procedures consist of two steps, "generic typing" and "subtyping". Generic typing, to determine serol. typing, was carried out using 12 probes with an amplified product using generic primer. Based on results of the first PCR-MPH generic typing, group specific amplification was performed followed by hybridization with sequence-specific oligonucleotides for subtyping. There were 7 probes for DR4 and 10 probes for DR6. This method enabled identification of generic type of DRB genes, 12 different alleles of DR4 and 16 different alleles of DR6.

L68 ANSWER 52 OF 54 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:127326 BIOSIS
DOCUMENT NUMBER: PREV200200127326
TITLE: **Oligonucleotide sizing** using **cleavable primers.**
AUTHOR(S): Monforte, J. A. [Inventor]; Becker, C. H. [Inventor]; Shaler, T. A. [Inventor]; Pollart, D. J. [Inventor]
CORPORATE SOURCE: Berkeley, Calif., USA
ASSIGNEE: SRI INTERNATIONAL
PATENT INFORMATION: US 5830655 Nov. 3, '1998
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 3, 1998) Vol. 1216, No. 1, pp. 536. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2002
Last Updated on STN: 26 Feb 2002
ED Entered STN: 30 Jan 2002
Last Updated on STN: 26 Feb 2002

L68 ANSWER 53 OF 54 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:88178 BIOSIS
DOCUMENT NUMBER: PREV200200088178
TITLE: **Oligonucleotide sizing** using immobilized **cleavable primers.**
AUTHOR(S): Monforte, J. A. [Inventor]; Becker, C. H. [Inventor]; Shaler, T. A. [Inventor]; Pollart, D. J. [Inventor]
CORPORATE SOURCE: Berkeley, Calif., USA
ASSIGNEE: SRI INTERNATIONAL
PATENT INFORMATION: US 5700642 Dec. 23, 1997
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 23, 1997) Vol. 1205, No. 4, pp. 3021. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2002
Last Updated on STN: 25 Feb 2002
ED Entered STN: 16 Jan 2002
Last Updated on STN: 25 Feb 2002

L68 ANSWER 54 OF 54 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000000434 EMBASE
TITLE: **Design** of PCR primers and gene probes for the general detection of bacterial populations capable of degrading aromatic compounds via catechol **cleavage** pathways.
AUTHOR: Sei K.; Asano K.-I.; Tateishi N.; Mori K.; Ike M.; Fujita M.
CORPORATE SOURCE: M. Fujita, Dept. of Environmental Engineering, Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan
SOURCE: Journal of Bioscience and Bioengineering, (1999) 88/5 (542-550).
Refs: 55
ISSN: 1389-1723 CODEN: JBBIF6
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB For the general detection of bacterial populations capable of degrading aromatic compounds, two PCR primer sets were designed which can, respectively, amplify specific fragments from a wide variety of catechol 1,2- dioxygenase (C120) and catechol 2,3-dioxygenase (C230) genes. The C120- targeting primer set (C120 primers) was designed based on the homologous regions of 11 C120 genes listed in the GenBank, while the C230-targeting one (C230 primers) was designed based on those of 17 known C230 genes. Oligonucleotide probes (C12Op and C23Op) were also designed from the internal homologous regions to identify the amplified fragments. The specificity of the primer sets and probes was confirmed using authentic bacterial strains known to carry the C120 and/or C230 genes used for the primer and probe design. Various authentic bacterial strains carrying neither C120 nor C230 genes were used as negative controls. PCR with the C12O primers amplified DNA fragments of the expected sizes from 5 of the 6 known C12O-carrying bacterial strains tested, and positive signals were obtained from 4 of the 5 amplified fragments on Southern

hybridization with the C12Op. The C23O primers amplified DNA fragments of the expected size from all the 11 tested C23O- carrying bacterial strains used for their design, while the C23Op detected positive signals in the amplified fragments from 9 strains. On the other hand, no DNA fragments were amplified from the negative controls. To evaluate the applicability of the designed primers and probes for the general detection of aromatic compound-degrading bacteria, they were applied to wild- type phenol- and/or benzoate-degrading bacteria newly isolated from a variety of environments. The C12O and/or C23O primers amplified DNA fragments of the expected sizes from 69 of the 106 wild-type strains tested, while the C12Op and/or C23Op detected positive signals in the amplified fragments from 63 strains. These results suggest that our primer and probe systems can detect a considerable proportion of bacteria which can degrade aromatic compounds via catechol cleavage pathways.

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